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Phytochemicals, pharmacological and ethnomedicinal studies of *Artocarpus*: A scoping review

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ABSTRACT

This article aims to review the scientific data on phytochemical and pharmacological studies of *Artocarpus* collected from Malaysia as well as to highlight their usage as ethnomedicine worldwide. About 55 *Artocarpus* species are distributed worldwide and 32 of the *Artocarpus* species can be found in Malaysia. *Artocarpus* species are well known worldwide for their edible fruits such as *Artocarpus heterophyllus* (jackfruit), *Artocarpus integer* (chempedak), and *Artocarpus communis* (breadfruit). Aside from its edible fruits, the timber is valued for light constructions, crates, large canoes, and boats. The literature for this review was searched using the term '*Artocarpus*', '*Artocarpus* Malaysia', '*Artocarpus* extracts', '*Artocarpus* traditional medicine' and '*Artocarpus* ethnomedicine' from published books and scientific journals *via* various engines such as The Web of Science, PubMed, Science Direct, Scopus, Research Gate, and Google Scholar. The references cited from the retrieved articles were also scanned and cross-checked. All published studies on phytochemical and pharmacological activities of Malaysia's *Artocarpus* species up to January 2021 were included in this review. Articles on phytochemical studies of Malaysia's *Artocarpus* revealed the isolation of flavonoids as the major constituents. Research on pharmacological activities of the isolated phytochemicals showed that these compounds exhibited significant disease-linked-enzyme (tyrosinase, cholinesterase, glucosidase) inhibitors as well as antioxidant, anti-inflammatory, antimicrobial, and cytotoxic activities. The ethnomedicinal data gathered are useful to understand and prioritize *Artocarpus* species that can contribute to potent phytochemicals and possibly new drug leads. This review also provides valuable information for the future development of isolated compounds from *Artocarpus* species.

KEYWORDS: *Artocarpus*; Phytochemistry; Pharmacological activities; Ethnomedicine; Flavonoids

1. Introduction

Genus *Artocarpus* is one of the important groups of plants that belongs to the Moraceae family. A total of 55 *Artocarpus* species spread throughout East Asia, South Asia, Southeast Asia to the New Guinea and southern Pacific[1,2]. Up to 2020, a total of 32 *Artocarpus* species and another two varieties were discovered in Malaysia[2–4]. Some *Artocarpus* species have edible fruits that led to cultivations for the products. The fruits can be eaten as soon as it is ripe. Most are eaten fresh after they are ripe, fried with batter, or served as desserts. The seed can also be eaten after boiling, baking, roasting, or frying[5]. Our investigation on *Artocarpus* species started since we did our own phytochemical and pharmacological research. Although several reviews on *Artocarpus* species had been published, the objectives and focus are very much different from this article[6,7].

In this article, we focus on reviewing the phytochemistry and pharmacological studies of *Artocarpus* species available in Malaysia. But before we dive into that, we need to know the distribution and availability of *Artocarpus* species in Malaysia. Then from this data, we gathered the reported ethnomedicinal usage from all around the world related to these *Artocarpus* species. The ethnomedicinal data are important to understand its relationship with the pharmacological activities tested[8]. All the data are tabulated in Table 1 for better understanding.

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2. Methodology

Literature was searched using various engines such as The Web of Science, PubMed, Science Direct, Scopus, Research Gate, and Google Scholar. The search term '*Artocarpus*', '*Artocarpus* Malaysia', '*Artocarpus* extracts', '*Artocarpus* traditional medicine' and '*Artocarpus* ethnomedicine' were used without limitations. The references cited from the retrieved articles were scanned and cross-checked. Other than published articles, information on *Artocarpus* species were also obtained from books published by reliable sources. The distribution, morphology, and ethnobotanical information of *Artocarpus* species were obtained from books published under the Ministry of Agriculture, Malaysia, and Forest Research Institute of Malaysia. All published researches on phytochemistry and pharmacological activities of Malaysia's *Artocarpus* species up to January 2021 were included in this review.

3. Morphology and distributions

Artocarpus trees are mostly evergreen with thick white latex. Their leaves are spirally arranged or alternate. While *Artocarpus* fruits have different sizes from small to large with fleshy seeds that are mostly large and embedded in the head of the fruit and surrounded by a waxy or pulpy succulent layer. The sapwood has various shades of light yellow which can be differentiated from the heartwood that has different shades of brown and sometimes traces of olive green. *Artocarpus* produces two types of hardwood, light and medium hardwood. Other than its edible fruits, *Artocarpus* is also well known for its valuable timber in Malaysia. The light hardwood timber is known as terap in Peninsular Malaysia and Sabah or pudau in Sarawak. The medium hardwood is known as keledang in Peninsular Malaysia, beruni in Sabah and selangking in Sarawak[2,3]. Kochummen identified 20 species of *Artocarpus* in Malaysia including two incompletely known species and reported in Tree Flora of Malaya[3]. Another book was published specifically for Sabah and Sarawak (East Malaysia) that confirmed the availability of 20 species with one incompletely known species[2]. These two reports conclude a total of 32 *Artocarpus* species and another two varieties in Malaysia. Distribution of identified *Artocarpus* in Malaysia is listed in Table 1.

4. Ethnomedicine

Ethnomedicine is the study of the cultural concept of health, disease and illness using nature[9]. There are several published articles on ethnomedicine practices using different parts of *Artocarpus* by certain tribes or specific locations in the world[10–16]. Table 1 highlights available *Artocarpus* species discovered in Malaysia including their ethnomedicine practices worldwide.

5. Phytochemistry

A total of 61 compounds were isolated from *Artocarpus* species collected from different locations in Malaysia. These compounds fall under the flavonoids (chalcones, flavones, flavanones, flavanols, flavonols), xanthones, stilbenoid as well as terpenoids, and sterols. Flavonoids are present in all *Artocarpus* species and proved to be the chemotaxonomic marker of *Artocarpus* plants. The structures of compounds 1-61 are shown in Supplementary Figures 1-5.

5.1. Phenolics secondary metabolites

5.1.1. Chalcones

Two separate studies of *Artocarpus lowii* (*A. lowii*) from Terengganu reported the isolation of two new dihydrochalcones. These chalcones are named as 2′,4′-dihydroxy-4-methoxy-3′-prenyldihydrochalcone (1) and 2′,4′-dihydroxy-3,4-(2″,2″-dimethylchromeno)-3′-prenyldihydrochalcone (2)[17,18]. Another two chalcones were also isolated and known as isobavachalcone (3) and 4-hydroxyonchocarpin (4)[17–19]. Isobavachalcone (3) was also isolated from *Artocarpus anisophyllus* (*A. anisophyllus*) collected from Johor[20]. In 2016, two new prenylated chalcones were reported from *A. lowii* collected from Selangor. These chalcones are identified as 2-hydroxyparatocarpin (5) and 2′,3,4′,4-tetrahydroxy-3′-prenylchalcone (6)[21]. A study on the leaves of *Artocarpus fulvicortex* (*A. fulvicortex*) from Terengganu, Malaysia gave 2′-hydroxy-4,4′,6′-trimethoxychalcone (7)[22]. In 2013, two new dihydrochalcones named elastichalcone A (8) and elastichalcone B (9) were isolated from the leaves of *Artocarpus elasticus* (*A. elasticus*) collected from Selangor, Malaysia[23]. The structures of all chalcones are presented in Supplementary Figure 1.

5.1.2. Flavones

Artonin E (10), a known flavone with four hydroxyl groups, a prenyl, and a chromeno ring was isolated from the barks of *Artocarpus scortechinii* (*A. scortechinii*), *Artocarpus teysmanii* (*A. teysmanii*), and *A. elasticus* from Selangor[24–27]. An investigation of *A. elasticus* in 2019 also reported a new diprenylated flavone, artoflavone B (11)[27]. In 2010, two new prenylated flavones were reported from two different species collected from Sarawak[28,29]. These flavones are named as artosimmin (12) from *Artocarpus odoratissimus* (*A. odoratissimus*) and hydroxyartocarpin (13) from the stem bark of *Artocarpus altilis* (*A. altilis*)[28,29]. Another three flavones isolated from *A. altilis* were identified as artocarpin (14), morusin (15), and cycloartocarpin A (16)[29]. Artochamin A (17), a prenylated pyranoflavone was isolated from the stem bark of *Artocarpus kemando* (*A. kemando*) also from Sarawak[30].

A thorough investigation on the leaves of *A. fulvicortex* from Terengganu gave a unique new flavone bearing two chromeno rings[22]. The structure was identified as 5-hydroxy-(6:7,3′:4′)-di(2,2-dimethylpyrano)flavone (18). Carpachromene (19) together

Table 1. Distribution and availability of *Artocarpus* species in Malaysia and their ethnomedicinal uses.

Species	Synonyms	Common/Local names	Distribution in Malaysia	Ethnomedicine practices worldwide	References
Artocarpus anisophyllus Miq.	*Artocarpus klidang* Boerl.; *Artocarpus superba* Becc.	Keledang babi, Terap ikal (Sabah), Bintau, Bintawak, Entawa, Mentawa, Kayo bibungan, Kelidang, Tawak (Sarawak)	West Malaysia (only available in Negeri Sembilan and Johor); East Malaysia (available widely in Sabah but uncommon in Sarawak)	–	[2,3]
Artocarpus anisophyllus var. *sessilifolius* Kochummen	–	Terap ikal	West Malaysia (not available); East Malaysia (widely distributed in Sabah but only single collection in Kuching Sarawak)	–	[2,3]
Artocarpus annulatus Jarrett	–	Bukoh, Patat	West Malaysia (not available); East Malaysia (only in Sarawak)	–	[2,3]
Artocarpus altilis Forsberg	*Artocarpus communis* J.R. & G. Forster; *Artocarpus camansi* Blanco; *Artocarpus incisus*	Sukun (Malay), Breadfruit (English)	Common, cultivated all over Malaysia	Leaves: Skin disease, toothache, enlarge spleen treatment (Indonesia); Diabetic treatment (Indonesia), eye ailments (Samoa and Futuna); Treatment of chest pain and vomiting that are caused by heart problem, muscle relaxant, remedy for fish poisoning (South Pacific) Shoots and flowers: Wrapped with *Macaranga dioica* leaves to treat migraine and headache (Vanuatu); Hemorrhoid treatment (Benin) Barks: Treatment for chest pain and vomiting that are caused by heart problem, bones pain, maternal postpartum infections (South Pacific), stomach aches, digestive tract problems (Samoa & Tonga), relapsed illness (Tonga); Treatment for stomach aches, heal wounds (Philippines); Treatment for measles, scabies, dysentery (Benin) Roots: Respiratory ailments include difficult & painful breathing, remedy for weakness after birth, blood vomiting and lung pain treatment (South Pacific); Treatment of diarrhea and dysentery (Indonesia); Treatment of typhoid fever, anaemia, malaria, regulation of blood pressure, heart palpitation (Benin) Seeds/Fruits: Help in giving birth, typhoid and other fever treatment (China); As aphrodisiac (Indonesia) Milky latex: Applied to rashes, abscesses, sores, wounds (Tonga and Tahiti); Dysentery treatment (Philippines); Mixed with equal amount of *Ficus adenosperm* latex to treat menorrhagia (Vanuatu) White sap: Treatment for eye puncture wounds (Micronesia)	[2,3,5–8,12,13,15]
Artocarpus corneri Kochummen	–	Talun	West Malaysia (not available); East Malaysia (only in Sarawak)	–	[2,3]
Artocarpus dadah Miq.	*Artocarpus mollis* Miq.; *Artocarpus rufescens* Miq.; *Artocarpus tampang* Miq.; *Artocarpus inconstantissima* Miq.; *Artocarpus lakoocha* Roxb.; *Artocarpus reniformis* Becc.; *Artocarpus dasyphylla* Miq	Tampang bulu (Peninsular), Beruni (Sabah), Dadah, dadak, meruni, selangking (Sarawak)	West Malaysia (common in lowland forest and open country/ villages throughout West Malaysia); East Malaysia (common in Sabah, rare in Sarawak)	Leaves: Treating oedema (Southeast Asia) Bark: Sap from bark used to clean leg wound (Indonesia) Juice and seed: As laxative (Myanmar) Roots: Tonic for deobstruent	[2,3,5,8]

Table 1. Distribution and availability of *Artocarpus* species in Malaysia and their ethnomedicinal uses (continued).

Species	Synonyms	Common/Local names	Distribution in Malaysia	Ethnomedicine practices worldwide	References
Artocarpus elasticus Reinw. ex Blume.	*Artocarpus blumei* Trec.; *Artocarpus kunstleri* King; *Artocarpus blumei* Trec.; *Artocarpus pubescens* Willd.; *Artocarpus sericicarpus* Jarrett.	Terap nasi, Terap togop (Sabah), Kian, Pedalai, Tekalong, Terap, Tian (Sarawak)	Common in lowland forest and open villages throughout West and East Malaysia	Leaves: Mix with rice and eaten for tuberculosis (Indonesia) Inner bark: As native bandages & poultice for ulcer (Malaysia) Bark: Pounded for lumbago (muscle and joint) treatment (Indonesia) Latex: Treatment for dysentery (inflammation of intestine) (Indonesia)	[2,3,5]
Artocarpus excelsus Jarrett	–	–	West Malaysia (not available); East Malaysia (rarely available in Sabah and Sarawak)	–	[2,3]
Artocarpus fulvicortex Jarrett	–	Tampang gajah	West Malaysia (only available in lowland forest of Perak, Pahang, Negeri Sembilan, Melaka); East Malaysia (not available)	–	[2,3]
Artocarpus glaucus Blume	*Artocarpus denisoniana* King	Merubi, Pudau putih, Selangking	West Malaysia (only available in lowland and hill forest of Kedah, Perak, Pahang, Selangor, Johor); East Malaysia (not available)	–	[2,3]
Artocarpus gomezianus Wall. ex Trec.	–	Tampang hitam	West Malaysia (only available in lowland forest of Kedah, Kelantan, Pahang, Negeri Sembilan, Johor); East Malaysia (not available)	–	[2,3]
Artocarpus heterophyllus Lamk.	–	Jackfruit (English), Nangka (Malay)	Commonly available because it is cultivated all over Malaysia	Sap: Antisyphilitic (Southeast Asia); Vermifuge (Southeast Asia); Ulcers, abscesses (Philippines, Myanmar, China) Pulp and seeds of fruits: Cooling tonic for pectoral muscle (Philippines, Myanmar, China) Leaves: Ulcers, wounds (Malaysia and Philippines); Increase milk secretion for woman (Southeast Asia) Barks: Ulcers (Malaysia); Sedative for convulsions (Southeast Asia); Applied on skin to reduce swelling (India) Roots: Diarrhoea (Myanmar); Fever (Malaysia)	[2,3,7,8,16]
Artocarpus hispidus Jarrett.	–	Temponek	West Malaysia (available in lowland forest of Penang, Perak, Pahang, Terengganu, Selangor); East Malaysia (not available)	–	[2,3]
Artocarpus integer Merr.	*Artocarpus chempeden* Spreng	Chempedak	Commonly available because it is cultivated all over Malaysia	Seeds: Treatment for diarrhea Roots: Treatment for malaria fever	[2,3,6]
Artocarpus integer var. *silvestris*	–	Bangkong	Widely distributed in Malaysia but nowhere abundant	–	[2,3]
Artocarpus jarriettiae Kochummen	–	Tekalong	West Malaysia (not available); East Malaysia (rarely available in Sabah and Sarawak)	–	[2,3]

Table 1. Distribution and availability of *Artocarpus* species in Malaysia and their ethnomedicinal uses (continued).

Species	Synonyms	Common/Local names	Distribution in Malaysia	Ethnomedicine practices worldwide	References
Artocarpus kemando Miq.	*Artocarpus brunneifolia* S. moore	Pudu (Sabah), Pudau, Selibut, Pupud, Puduh, Puroh (Sarawak)	West Malaysia (commonly available in lowland forest of Terengganu, Pahang, Selangor); East Malaysia (available widely in Sabah and Sarawak)	–	[2,3]
Artocarpus lanceifolius Roxb.	–	Keledang	Widely distributed in Malaysia but nowhere abundant	–	[2,3]
Artocarpus lowii King	–	Miku	Widely distributed in Malaysia but nowhere abundant	–	[2,3]
Artocarpus maingayi King	–	Pudu	Available in lowland forest throughout Malaysia	–	[2,3]
Artocarpus melinoxylus Gagnep.	–	Pala mansoh, Pala tupai, Temponek	West Malaysia (not available); East Malaysia (rarely available in Sabah and Sarawak)	–	[2,3]
Artocarpus nitidus Trec.	*Artocarpus lanceolate* Trec.; *Artocarpus humilis* Becc.; *Artocarpus lamellose* Blanco.; *Artocarpus sampor* Gagnep.; *Artocarpus lingnanensis*; *Artocarpus borneensis* Merr.; *Artocarpus gomeziana* Wall.; *Artocarpus griffithii* Merr.	Tampang (Peninsular), Selangking, Beruni (Sabah), Dadak, Empaka, Karon, Ngidinuk, Sinojoh, Taburakin (Sarawak)	Available in lowland forest throughout Malaysia	–	[2,3]
Artocarpus obtusus Jarrett	–	Sarawak and Sabah	–	–	[2,3]
Artocarpus odoratissimus	*Artocarpus tarap* Becc.; *Artocarpus mutabilis* Becc.	Marang/Terap, Timadang (Sabah), Keiran Pingan Tekalong (Sarawak)	West Malaysia (cultivated throughout West Malaysia); East Malaysia (growing naturally in Sabah and Sarawak)	Latex: Treat inflammation from wounds (Malaysia)	[2,3]
Artocarpus peltatus Merr.	–	–	West Malaysia (not available); East Malaysia (commonly available in Sarawak but rarely available in Sabah)	–	[2,3]
Artocarpus primackiana Kochummen	–	Beruni (Sabah), Dadah (Sarawak)	West Malaysia (not available); East Malaysia (rarely available in Sabah and Sarawak)	–	[2,3]
Artocarpus rigidus Blume	*Artocarpus rotunda*; *Artocarpus cuspidatus*; *Artocarpus kertau*; *Artocarpus varians* Miq; *Artocarpus dimorphophylla* Miq.	Temponek	Widely distributed throughout Malaysia	–	[2,3]

Table 1. Distribution and availability of *Artocarpus* species in Malaysia and their ethnomedicinal uses (continued).

Species	Synonyms	Common/Local names	Distribution in Malaysia	Ethnomedicine practices worldwide	References
Artocarpus sarawakensis Jarrett	–	Pedalai, pingan (Sarawak)	West Malaysia (not available); East Malaysia (rarely available in Sarawak)	–	[2,3]
Artocarpus scortechinii King	–	Terap hitam	Scattered throughout Malaysia	–	[2,3]
Artocarpus tamaran Becc.	–	Timbangan (Sabah), Kakang, tamaran, tembaran, kalong, kihan (Sarawak)	West Malaysia (not available); East Malaysia (rarely available in Sabah and Sarawak)	–	[2,3]
Artocarpus teysmannii Miq.	*Artocarpus peduncularis*	Chempedak ayer	West Malaysia (available in Perak and Selangor); East Malaysia (available in Sabah and Sarawak)	–	[2,3]
Artocarpus tomentosulus Jarrett	–	–	West Malaysia (not available); East Malaysia (rarely available in Sabah)	–	[2,3]
Artocarpus sp. 'A'	–	Tampang FRI 17082 (Known from only one collection)	West Malaysia (Gunung Tampin, Negeri Sembilan)	–	[2,3]
Artocarpus sp. 'B'	–	Tampang FRI 19234 (Known from only one collection)	West Malaysia (Gunung Ledang, Johor)	–	[2,3]
Artocarpus sp. A	–	SAN 82081 (Known from only one collection)	East Malaysia (Sepilok, Sandakan Sabah)	–	[2,3]

with cycloartocarpesin (20) and norartocarpetin (21) was isolated from *A. fulvicortex*[22]. Cycloartocarpesin (20) was also reported in a phytochemical study of *A. elasticus* from Selangor[23].

In 2015, two new and three known flavones were isolated from *A. anisophyllus* collected from Johor[20]. The new flavones were identified as 4′,5-dihydroxy-6,7-(2,2-dimethylpyrano)-2′-methoxy-8-γ,γ-dimethylallylflavone (22) and 3-hydroxycycloartocarpin (23) while the others are known as artocarpin (14), cycloartocarpin (24), and chaplashin (25)[20]. The following year, Abdullah *et al.* reported the isolation of artocarpin(14), 4′,5-dihydroxy-6,7-(2,2-dimethylpyrano)-2′-methoxy-8-γ,γ-dimethylallylflavone (22), and cycloheterophyllin (26) from *A. lowii*[18]. Whilst Arriffin *et al.* reported the isolation of 4′,5-dihydroxy-6,7-(2,2-dimethylpyrano)-2′-methoxy-8-γ,γ-dimethylallylflavone (22) from the bark of *A. scortechinii* in 2017[31]. Methoxycyclocommunol (27), cyclocommunol (28), and cudraflavone C (29) were present in the bark of *Artocarpus integer* var. *silvestris* (*A. integer* var. *silvestris*) from Pahang[32]. The structure of methoxycyclocommunol (27) was reported as a new derivative of cyclocommunol (28) due to the presence of a sharp peak indicating methoxy group in ^{1}HNMR.

5.1.3. Flavanones

Two flavanones were reported for the first time from *Artocarpus* species characterized as 5,7-dihydroxy-4′-methoxy-8-prenylflavanone (30) and 5-hydroxy-7,8-(2,2-dimethylchromano)-4′-methoxyflavanone (31)[20,33]. In 2016, a phytochemical study on *A. integer* var. *silvestris* yielded heteroflavanone A (32) whilst two common flavanones named pinostrobin (33) and pinocembrin (34) were obtained from *A. odoratissimus*[32,34].

5.1.4. Flavanols

Flavanols are also referred to as dihydroflavonols. Shah *et al.* obtained a common flavanol named catechin (35) from the leaves of *A. fulvicortex* collected from Terengganu[35]. Arriffin *et al.* reported the isolation of two new dihydroflavonols named artoscortonol A (36) and artoscortonol B (37) from the leaves of *A. scortechinii*[36]. The structures of all flavanones (30-34) and flavanols (35-37) are presented in Supplementary Figure 3.

5.1.5. Xanthones and stilbenoid

Several articles reported the isolation of artobiloxanthone (38), cycloartobiloxanthone (39), and artonol B (40) from the barks of *A. scortechinii* and *A. teysmanii*[24,25,31]. Two separate study by Ee *et al.* and Hashim *et al.* on *A. kemando* from Sarawak also isolated cycloartobiloxanthone (39) and artonol B (40)[30,37]. In addition, Ee *et al.* highlights another two xanthones named as artomandin (41),

and artoindonesianin C (42) from *A. kemando*[30]. The first chemical investigation on the stem bark of *A. obstusus* in 2010 by Hashim *et al.* found two new xanthones named pyranocycloartobiloxanthone A (43) and dihydroartoindonesianin C (44)[38]. Afterwards, Hashim *et al.* reported the isolation of pyranocycloartobiloxanthone B (45) from *A. obstusus* and dihydroartoindonesianin C (44) from *A. kemando*[37,39].

In 2015, Lathiff *et al.* obtained pyranocycloartobiloxanthone A (43) from a rare *Artocarpus* species identified as *A. anisophyllus*[20]. The following year, a known xanthone called artonin F (46) was reported from *A. integer* var. *silvestris* from Pahang whereas the investigation on the stem bark of *A. altilis* yielded two known xanthones, cycloartobiloxanthone (39) and artoindonesianin Ⅴ (47)[29,32]. An extensive investigation on *A. elasticus* in 2016 reported a new xanthone named elastixanthone (48) together with artobiloxanthone (38) and cycloartobiloxanthone (39)[26]. A recent investigation on *A. elasticus* in 2019 also reported the isolation of artobiloxanthone (38) and cycloartobiloxanthone (39), elastixanthone (48) as well as artoindonesianin P (49)[27]. Isolation of a common stilbenoid, oxyresveratrol (50) was reported from *A. scortechinii* and *A. fulvicortex*[31,35]. The structures of xanthones and stilbenoid (38-50) are presented in Supplementary Figure 4.

5.2. Other types of secondary metabolites

Isolation of friedelin (51), lupeol (52), and lupeol-3-acetate (53) was reported from separate study on *A. fulvicortex* from Terengganu[22,35]. A recent study showed *A. odoratissimus* roots contained two terpenoids, α and β amyrin acetate (54, 55)[34]. The structures can be distinguished from proton NMR and by comparison with literature. Traxateryl acetate (56) was also isolated from the stem bark and the roots of *A. odoratissimus* together with hexyl dodecanoate (57)[28,34]. Two common sterols, β-sitosterol (58) and stigmasterol (59) were reported from *A. kemando* and *A. odoratissimus*[29,34]. Phytochemical studies on the stem bark of *A. kemando* from Sarawak yielded 6,7-dimethoxycoumarin (60) and aurantiamide benzoate (61). Aurantiamide benzoate (61) was reported as the first dipeptide isolated from genus *Artocarpus*. It was crystallized from chloroform extracts of *A. kemando*'s stem bark after a series of purification processes[37]. Structures of other secondary metabolites are shown in Supplementary Figure 5.

6. Pharmacological activities

The *Artocarpus* species have been exploited in various countries and revealed the medicinal variation possibility. As noted earlier, the most common ethnomedicinal usage was to treat wounds and ulcers as well as some skin problems. Extensive literature reported different pharmacological tests involved with the extracts and the isolated phytochemicals which exhibited anti-inflammatory, antioxidant, antimicrobial, gastroprotective, cytotoxic, anti-proliferative activities and acted as selective enzymes inhibitors. Qualitative and quantitative phytochemical screening of the *Artocarpus* extracts revealed their high phenolic content[40–45].

6.1. Antioxidant activities

Several reports have revealed the positive correlation between high phenolic content and the antioxidant activities of the crude extracts and fractions[40,42–45]. Antioxidant activity for isolated compounds also had been reported. 2′,4′-Dihydroxy-4-methoxy-3′-prenyldihydrochalcone (1), isobavachalcone (3) and 4-hydroxyonchocarpin (4) from *A. lowii* showed strong free radical scavenging activities against 2,2′-diphenyl-1-picrylhydrazyl (DPPH) with 50% inhibition (scavenging) concentrations (IC_{50}) of 0.03-0.24 mM using electron spin resonance spectrometry[17]. Ferric reducing antioxidant power assay (FRAP), 2,2′-azino-bis (3-ethylbenzthiazoline-6-sulfonic acid) (ABTS) and DPPH scavenging assays for all the isolates, 2′,4′-dihydroxy-4-methoxy-3′-prenyldihydrochalcone (1), 2′,4′-dihydroxy-3,4-(2″,2″-dimethyl-chromeno)-3′-prenyldihydrochalcone (2), isobavachalcone (3), 4-hydroxyonchocarpin (4), artocarpin (14), and cycloheterophyllin (26) from *A. lowii* were also conducted. Cycloheterophyllin (26) gave promising results compared with standards, butylated hydroxyanisole (BHA) with 50% scavenging concentration (SC_{50}) values of 0.320 mM (BHA=0.554 mM) (ABTS), 0.10 mM (BHA=0.082 mM) (DPPH) and (4.70±0.09) [Trolox=(2.8±0.09)] FRAP equivalent[19]. New chalcones, elastichalcones A-B (8-9) and cycloartocarpesin (20) from *A. elasticus* were tested using Thin Layer Chromaography (TLC) bioautography method for DPPH scavenging activity. Elastichalcone B (9) and cycloartocarpesin (20) showed colour changes and further evaluation using 96-wells with a microplate photometer supported the TLC results with IC_{50} values of 11.30 and 11.89 μg/mL respectively[23].

Pyranocycloartobiloxanthone A (43) was obtained from *Artocarpus obstusus* for the first time together with dihydroartoindonesianin C (44) and pyranocycloartobiloxanthone B (45). Although they have similar backbones, only pyranocycloartobiloxanthone A (43) showed promising results against DPPH radical with IC_{50} of 2.0 μg/mL while the other xanthones were considered inactive with IC_{50} more than 500 μg/mL[38,39]. Isobavachalcone (3), artocarpin (14), 4′,5-dihydroxy-6,7-(2,2-dimethylpyrano)-2′-methoxy-8-γ,γ-dimethylallylflavone (22), 5,7-dihydroxy-4′-methoxy-8-prenylflavanone (30), 5-hydroxy-7,8-(2,2-dimethylchromano)-4′-methoxyflavanone (31) and pyranocycloartobiloxanthone A (43) from *A. anisophyllus* were tested using DPPH scavenging assay with a microplate photometer. Pyranocycloartobiloxanthone A (43) demonstrated strong antioxidant activity with SC_{50} of 20.2 μg/mL comparable with the positive control, BHA (SC_{50}=17.5 μg/mL)[20]. The structure activity relationship between flavonoids artosimmin (12), cycloartobiloxanthone (39), artonol B (40), artomandin (41),

artoindonesinin C (42) and extracts of *A. odoratissimus* and *A. kemando* was evaluated using DPPH radical scavenging assay. All extracts of *A. odoratissimus* exhibited weak inhibition activity (>120 μg/mL) compared with *A. kemando* (<55 μg/mL). Artomandin (41) and artosimmin (12) from *A. kemando* exhibited the highest potential in DPPH radical scavenging assay with IC_{50} of 38.0 and 32.1 μg/mL respectively[46]. The antioxidant capacities of *Artocarpus* secondary metabolites and extracts might lead to alleviation of diabetes mellitus and link to inhibition of tumour or cancer cell with potential anti-proliferative activities[47,48].

6.2. Anti-inflammatory activity

The anti-inflammatory activity of 2′,4′-dihydroxy-4-methoxy-3′-prenyldihydrochalcone (1), isobavachalcone (3), 4-hydroxyonchocarpin (4), and cycloheterophyllin (26) from *A. lowii* was investigated using cyclooxygenase-2 (COX-2) and 15-lipoxygenase (15-LOX) screening kit. Isobavachalcone (3) was found to possess potent anti-inflammatory activity *via* COX-2 mechanism (IC_{50}=0.95 μM). However, no activities were shown by other compounds towards COX-2 and 15-LOX[49]. In 2017, seven flavonoids *i.e.* 2′,4′-dihydroxy-4-methoxy-3′-prenyldihydrochalcone (1), isobavachalcone (3), artonin E (10), artocarpin (14), 4′,5-dihydroxy-6,7-(2,2-dimethylpyrano)-2′-methoxy-8-γ,γ-dimethylallylflavone (22), cycloheterophyllin (26) and oxyresveratrol (50) from several *Artocarpus* species were investigated on inhibitory effect against the production of prostaglandin E_2 (PGE_2) in human plasma. The level of PGE_2 in plasma was determined using radioimmunoassay technique. Artocarpin (14) showed the highest inhibition of 68.1% followed by artonin E (10) (66.8%) compared with the positive control, indomethacin (79.2%). 2′,4′-Dihydroxy-4-methoxy-3′-prenyldihydrochalcone (1), artonin E (10), artocarpin (14), and 4′,5-dihydroxy-6,7-(2,2-dimethylpyrano)-2′-methoxy-8-γ,γ-dimethylallylflavone (22) were the most potent inhibitors with IC_{50} values of 8.99 μM, 8.98 μM, 11.66 μM, and 7.04 μM, respectively (indomethacin: IC_{50}=2.27 μM). These compounds reduced PGE_2 production in human blood which directly inhibited COX-2 enzymatic activity[50]. Isolated compounds methoxycyclocommunol (27), cyclocommunol (28), cudraflavone C (29), heteroflavanone A (32), and artonin F (46) from *A. integer* var. *silvestris* were tested for their anti-inflammatory activity using 15-LOX screening kit and inhibitory effects on production of PGE_2 in whole blood. All compounds showed weak inhibition against 15-LOX even at a concentration of 100 μM. Only methoxycyclocommunol (27), cudraflavone C (29), heteroflavanone A (32), and artonin F (46) were screened for inhibitory effects on production of PGE_2 in whole blood using radioimmunoassay methods. All compounds except artonin F (46) showed more than 55% inhibition which then proceeded to serial dilution method to determine the IC_{50} value. Cudraflavone C (29) showed the most potent COX-2 inhibition on PGE_2 with IC_{50} of 0.07 μM which showed lower concentration needed for 50% inhibition compared with the positive control, indomethacin (IC_{50}=0.2 μM). Methoxycyclocommunol (27) and heteroflavanone A (32) also showed remarkable COX-2 inhibition on PGE_2 with IC_{50} values of 4.3 and 0.8 μM, respectively[32]. These results indicated that isolated flavonoids from *Artocarpus* do not respond towards 15-LOX mechanisms but act as selective inhibitors through COX-2 pathway.

6.3. Antimicrobial activity

Pyranocycloartobiloxanthone A (43), dihydroartoindonesianin C (44), and pyranocycloartobiloxanthone B (45) were screened for their antimicrobial properties using disc diffusion method. Only pyranocycloartobiloxanthone A (43) showed inhibition against most of the bacteria and fungi tested. Among all the microbes, pyranocycloartobiloxanthone A (43) showed the most promising result against methicillin resistant *Staphylococcus aureus* (*S. aureus*) (MRSA) with a 20 mm inhibition zone. Dihydroartoindonesianin C (44), and pyranocycloartobiloxanthone B (45) were found to be inactive[39]. Pyranocycloartobiloxanthone A (43) was also tested against two strains of *Helicobacter pylori*, NCTC 11637 (ATCC 43504) and J99 (ATCC 700824) with MIC values of > 250 μg/mL and 62.5 μg/mL, respectively. *Helicobacter pylori* is a bacterium that can cause ulcers in the stomach[51].

Crude extracts and ten isolated flavonoids, 2′,4′-dihydroxy-4-methoxy-3′-prenyldihydrochalcone (1), 2′,4′-dihydroxy-3,4-(2″,2″-dimethylchromeno)-3′-prenyldihydrochalcone (2), isobavachalcone (3), 4-hydroxyonchocarpin (4), artocarpin (14), 4′,5-dihydroxy-6,7-(2,2-dimethylpyrano)-2′-methoxy-8-γ,γ-dimethylallylflavone (22), cycloheterophyllin (26), 5,7-dihydroxy-4′-methoxy-8-prenylflavanone (30), 5-hydroxy-7,8-(2,2-dimethylchromano)-4′-methoxyflavanone (31) and pyranocycloartobiloxanthone A (43) from *A. lowii* and *A. anisophyllus* were screened for antimicrobial activities against four bacteria (*Bacillus subtilis*, *S. aureus*, *Escherichia coli*, *Pseudomonas putida*) and two fungi (*Candida albicans*, *Candida glabrata*) *via* disc diffusion method and determination of minimum inhibitory concentration as well as minimum microbicidal concentration. The crude extracts showed inhibition against Gram-positive bacteria but a negative response toward fungi. Artocarpin (14) showed the most promising result as an antimicrobial agent with more than 11 mm inhibition zone and a minimum microbicidal concentration value of 0.45 mg/mL[19].

In 2015, ultrastructural changes of *S. aureus* were compared against artonin E (10) and streptomycin (positive control) using two methods, standard antimicrobial technique, and transmission electron microscopy. The minimum inhibitory concentration of 3.9 μg/mL and minimum microbicidal concentration of 7.81 μg/mL against *S. aureus* proved that artonin E (10) is active against Gram-positive bacteria. In addition, the transmission electron microscope images of *S. aureus* before and after artonin E (10) treatment were shown and the original shape, cocci colonies of grape shape walls were missing, shredded and broken which led to distorted shape and focally thickened outer membrane indicating severe damage[52].

6.4. Tyrosinase inhibitory activity

Preliminary screening of pyranocycloartobiloxanthone A (43) from *Artocarpus obtusus* showed significant tyrosinase inhibitory activity with 80% inhibition comparable to kojic acid with 96% inhibition[39]. Further investigation by Lathiff *et al.* proved that aside from acting as a potent antioxidant, pyranocycloartobiloxanthone A (43) also acted as a tyrosinase inhibitor with IC_{50} of 60.5 μg/mL (kojic acid = 31.2 μg/mL)[20]. As expected, the ethyl acetate extract of *A. anisophyllus* heartwood where the compound was isolated exhibited a low IC_{50} value (155.4 μg/mL). Other isolated flavonoids *i.e.* isobavachalcone (3), hydroxyartocarpin (13), artocarpin (14) and 4′,5-dihydroxy-6,7-(2,2-dimethylpyrano)-2′-methoxy-8-γ,γ-dimethylallylflavone (22) were also evaluated for their inhibitory effect against tyrosinase enzyme *in vitro* with IC_{50} values of more than 200 μg/mL[20]. Cycloheterophyllin (26) from *A. lowii* demonstrated significant tyrosinase inhibitory activity against mushroom tyrosinase with IC_{50} of 52.5 μg/mL comparable with the positive control, kojic acid (IC_{50}=31.2 μg/mL). Other flavonoids 2′,4′-dihydroxy-4-methoxy-3′-prenyldihydrochalcone (1), 2′,4′-dihydroxy-3,4-(2″,2″-dimethylchromeno)-3-prenyldihydrochalcone (2), isobavachalcone (3), 4-hydroxyonchocarpin (4), artocarpin (14), and 4′,5-dihydroxy-6,7-(2,2-dimethylpyrano)-2′-methoxy-8-γ,γ-dimethylallylflavone (22) were also tested but found inactive[53].

6.5. Cholinesterase inhibitory activity

Isobavachalcone (3), 5,7-dihydroxy-4′-methoxy-8-prenylflavanone (30) and 5-hydroxy-7,8-(2,2-dimethylchromano)-4′-methoxyflavanone (31) from *A. anisophyllus* were selected for *in silico* bioactivity analysis. 5,7-Dihydroxy-4′-methoxy-8-prenylflavanone (30) was found nontoxic in absorption, digestion, metabolism, and excretion study. 5,7-Dihydroxy-4′-methoxy-8-prenylflavanone (30) also followed the drug-likeness properties in Molsoft described by Lipinski Rule of 5 (RO5) for orally administered drugs. In this study, acetylcholinesterase (AChE) was chosen as target while 5,7-dihydroxy-4′-methoxy-8-prenylflavanone (30) as ligand. Molecular docking was performed between ligand and target along with known inhibitors and drug molecules available on the market. The docking score of ligand-target binding complex (−13.576 2) was more significant than phase 4 drugs but lower than donepezil (−15.497 4) and some other known inhibitors. The IC_{50} value for 5,7-dihydroxy-4′-methoxy-8-prenylflavanone (30) was 1 659 nM against AChE in QSAR analysis. *In vitro* experiment was done to validate the *in silico* result using TLC bioautographic method and 5,7-dihydroxy-4′-methoxy-8-prenylflavanone (30) showed potential as an AChE inhibitor with a detection limit of 125 μg/mL[33].

Dichloromethane and methanol extracts of *A. fulvicortex* heartwoods demonstrated AChE inhibitory activity with a detection limit of 2 mg/mL. Catechin (35) and oxyresveratrol (50) from *A. fulvicortex* exhibited moderate AChE inhibitory activity using TLC bioautographic method and microplate assay. Oxyresveratrol (50) acted as a potent inhibitor with IC_{50} value of 6.25 mM comparable to galanthamine as a positive control[35]. In 2019, cholinesterase inhibition screening of methanol extracts of *A. altilis* and *A. integer* leaves against AChE and BChE at 200 μg/mL was done with physostigmine as the positive control. Both species showed inhibition percentage of more than 80%. Further investigation revealed acidic fraction (*via* acid-base fractionation of methanol extract) of *A. altilis* leaves showed higher inhibition compared to ethyl actetate fraction (*via* liquid-liquid fractionation of methanol extract)[54].

6.6. Alpha glucosidase activity

Six compounds from *A. elasticus* were screened using alpha glucosidase-UV assay. Artonin E (10), artoflavone B (11) and four dihydrobenzoxanthone known as artobiloxanthone (38), cycloartobiloxanthone (39), elastixanthone (48) and artoindonesianin P (49) showed promising results as alpha glucosidase inhibitors with IC_{50} between 7.6-25.4 μM. Overall, all compounds showed dose dependent inhibition of enzyme. A detailed kinetic analysis on the inhibition of artobiloxanthone (38), cycloartobiloxanthone (39), elastixanthone (48) and artoindonesianin P (49) was carried out using double reciprocal plots. These analyses determined the kinetic profile of elastixanthone (48) with IC_{50} value of 7.6 μM as a slow binding inhibitor due to the residual activity of the enzyme which decreases as a function of preincubation time. Molecular docking was also conducted between *Saccharomyces cerevisiae* alpha-glucosidase and the xanthones as ligand. The docking results revealed that all compounds have similar binding confirmations stabilized by interactions[27].

6.7. Cytotoxicity

Cytotoxicity in natural product is an important aspect to be measured as it requires to produce effects only on targeted cells without harming the host[55]. Artosimmin (12) and artomandin (41) exhibited strong inhibition activity against HL-60 human promyelocytic leukemia with IC_{50} of 1.1 and 2.4 μg/mL, respectively, and against MCF-7 human breast adenocarcinoma cancer cell with IC_{50} of 3.4 and 3.1 μg/mL, respectively[28,30]. The cytotoxicity of *A. odoratissimus* ethanol fruit extract was tested against human liver cancer cells (HepG2), human colon cancer cells (HT-29), and human ovarian cancer cells (Caov3) and was found inactive towards all tested cells[41]. *A. altilis* methanol pulp extract showed some toxicity against HeLa cells with IC_{50} of 50 μg/mL. Cell proliferation and viability decreased as the concentration of the *A. altilis* methanol pulp extract increased[56].

Pyranocyloartobiloxanthone A (43) exhibited strong antiproliferative activity against K562 human chronic myeloid leukemia cell with IC_{50} of 0.5 μg/mL and moderate inhibition against HL-60 human promyelocytic leukemia cell with IC_{50} of 2.0 μg/mL and MCF7 positive breast cancer cell with IC_{50} of 5.0 μg/mL in MTT assay[57]. Pyranocycloartobiloxanthone A (43) showed significant

gastroprotective efficacy using ethanol-induced ulcer model in rats. The 50% lethal dosage (LD_{50}) value of pyranocycloartobiloxanthone A (43) was more than 300 mg/kg in acute toxicity analysis. The possible side effect to other organs was also analyzed using liver function test. This study revealed that pre-treatment with pyranocycloartobiloxanthone A (43) significantly protects and reduces gastric mucosa from ethanol-induced gastric lesions as well as restores the depleted gluthione, non-protein sulfhydryl compound and nitric oxide levels in gastric homogenate[51].

Several pieces of research were conducted to investigate the cytotoxicity and inhibitory mechanism of artonin E (10) towards ovarian and breast cancer cells. Rahman *et al.* reported that artonin E (10) induced antiproliferative effect that led to S phase cell cycle arrest in a time-dependent manner and apoptosis by dysregulating mitochondrial pathways in SKOV-3 ovarian cancer cells[58]. Antiproliferative effects of artonin E (10) on various cell lines were evaluated using MTT assay. The IC_{50} value for human ovarian adenocarcinoma cells (SKOV-3) was dramatically decreased after 24 h, comparable to the positive control, carboplatin, and paclitaxel. However, the normal human ovarian surface epithelial cells (T1074) showed more resistance towards artonin E. Artonin E also showed potential to inhibit aggressive triple-negative breast cancer cell (MDA-MB-231) by effectively reducing the apoptosis evading capacity, causing a half-maximal growth inhibition at low concentrations (14.3, 13.9 and 9.8 μM) after 24, 48 and 72 h respectively[59]. Furthermore, artonin E (10) helped in delaying quadruple tumor growth by more than 5 days compared to the untreated control group in female mice bearing 4T1 mammary tumors[60].

An *in vitro* study demonstrated jacalin, a lectin purified from protein extracts of *Artocarpus heterophyllus* seeds inhibited the viability of cancer cell MCF7 and H1299. The cancer cell viability was significantly decreased within 24 h upon treatment with purified and standard jacalin. The difference of 10% of cell viability between the purified jacalin and the extracts showed that it is necessary to purify the protein extract. At the highest concentration (10 μL), the purified and standard jacalin showed almost equal proliferation activity with only 0.98% difference[61].

6.8. Other pharmacological activities

Isolated compounds, 2′,4′-dihydroxy-4-methoxy-3′-prenyldihydrochalcone (1), isobavachalcone (3), artonin E (10), cycloheterophyllin (26), artobiloxanthone (38), cycloartobiloxanthone (39) and artonol B (40) from *A. lowii*, *A. scortechinii*, and *A. teysmanii* were investigated for their ability to inhibit arachidonic acid, collagen, and adenosine diphosphate–induced platelet aggregation in human whole blood. Cycloheterophyllin (26) inhibited arachidonic acid with IC_{50} of 100.9 μM and showed strong inhibition against adenosine diphosphate-induced aggregation with IC_{50} of 57.1 μM[62].

7. Conclusions and recommendations

This review highlights the phenolic compounds from selected *Artocarpus* in Malaysia, as well as their pharmacological activities. To date, 61 distinct compounds had been isolated from Malaysia's *Artocarpus* and 18 were reported as new ones. Although there are 32 *Artocarpus* species identified in Malaysia, the published articles showed that research in Malaysia focuses on twelve *Artocarpus* species *i.e. A. altilis*, *A. anisophyllus*, *A. elasticus*, *A. fulvicortex*, *Artocarpus heterophyllus*, *A. integer* var. *silvestris*, *A. kemando*, *A. lowii*, *Artocarpus obtusus*, *A. odoratissimus*, *A. scortechinii* and *A. teysmanii*. Based on literature review, *A. altilis* is the most widely utilized *Artocarpus* species. Data gathered highlights the potential of *Artocarpus* as an important source of secondary metabolites to inhibit a certain enzyme, and act as antioxidant, antimicrobial, anti-inflammatory as well as cytotoxic and gastroprotective agents.

Further research such as *in silico* and *in vivo* assay is recommended for better understanding on how the isolated natural products work. Only two *in silico* studies of *Artocarpus* from Malaysia were conducted and valuable data were gathered[27,33]. Pro-oxidant activity of isolated compounds in the presence of copper ions may also be explored as there are evidence associated with anticancer activity[63]. Furthermore, other parts of the plant such as flower can also be explored as there are recent articles that highlighted the flower of *Artocarpus lakoocha* and *Artocarpus heterophyllus* as a source of bioactive compounds[55].

Conflict of interest statement

We declare that there is no conflict of interest.

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Authors' contributions

SMAL and SJ created the concept and designed the structural

and intellectual content. SMAL as the main author involved in the preparation and review of the manuscript. Both SMAL and SJ also involved in the final version of the manuscript. While SMAL and NMA contributed to literature search, data and statistical analysis as well as manuscript editing. SJ as a corresponding author also acted as a guarantor and supervised the project.

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Phytochemicals, Pharmacological and Ethnomedicinal Studies of *Artocarpus*: A Scoping Review

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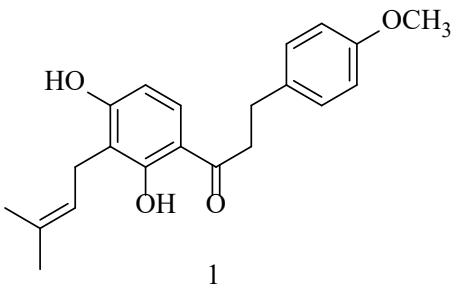

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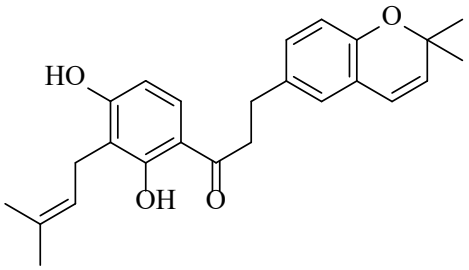

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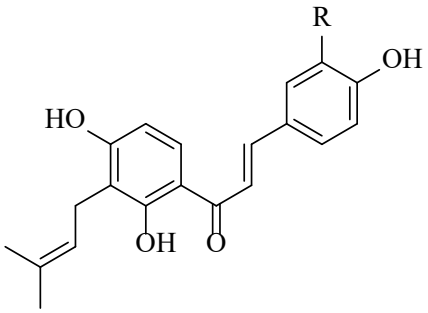
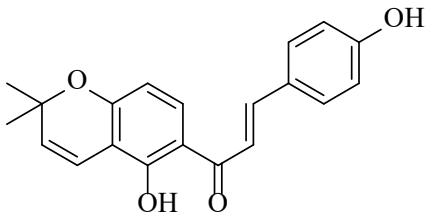
2',4'-Dihydroxy-3,4-(2",2"-dimethylchromeno)-3',-prenyldihydrochalcone



3: R = H ; Isobavacalcone
6: R = OH; 2',3,4',4-Tetrahydroxy-3'-prenylchalcone



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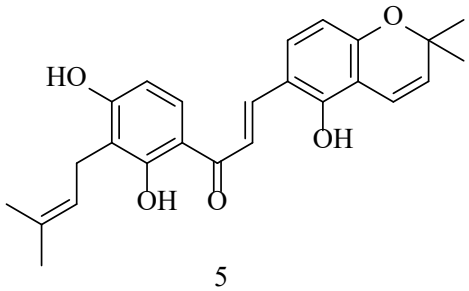
4-Hydroxyonchocarpin



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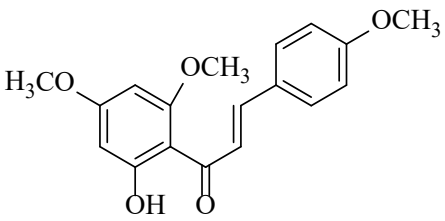
2-Hydroxyparatocarpin



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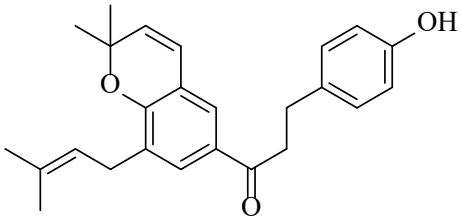
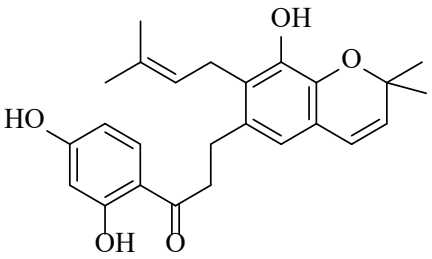
2'-Hydroxy-4,4',6'-trimethoxychalcone



8

Elastichalcone A



9

Elastichalcone B

Supplementary Figure 1: Chalcones isolated from Malaysia's *Artocarpus*

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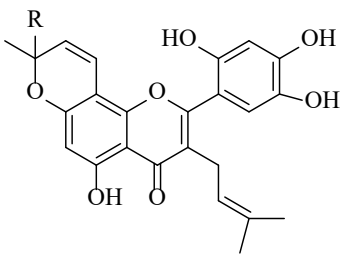
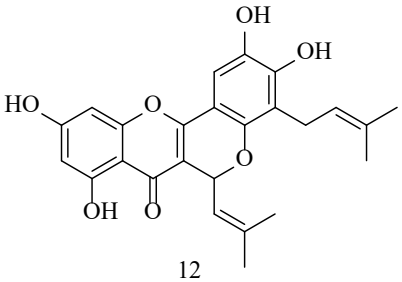


10: R= CH_3; Artonin E
11: R= Prenyl; Artoflavone B



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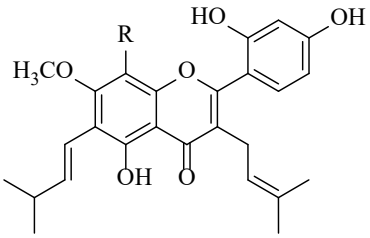
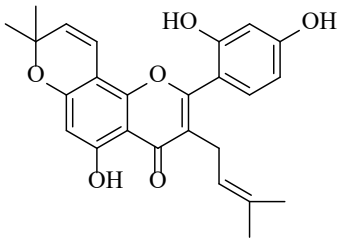
Artosimmin



13: R = OH; Hydroxyartocarpin
14: R = H; Artocarpin



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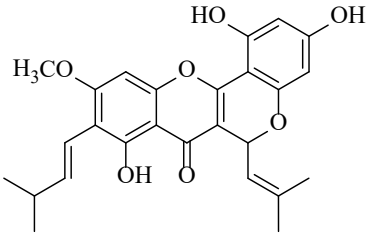
Morusin



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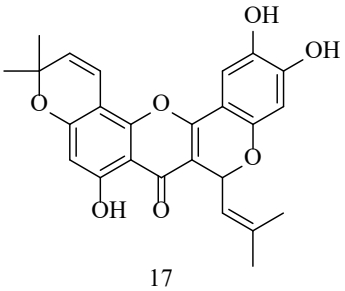
Cycloartocarpin A



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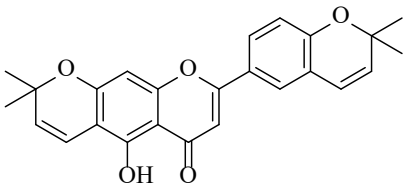
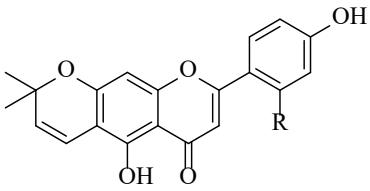
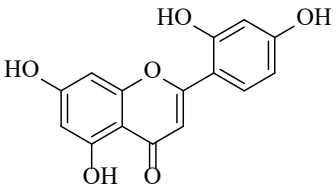
Artochamin A



18
5-hydroxy-(6:7,3':4')-di(2,2-dimethyl-pyrano)flavone



19: R = H; Carpachromene
20: R = H; Cycloartocarpesin



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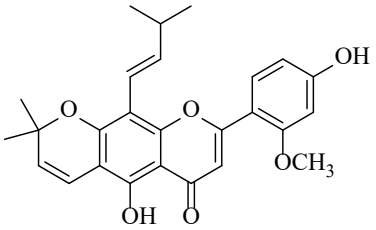
Norartocarpetin



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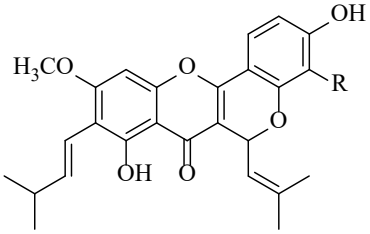
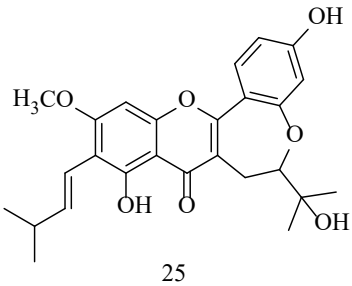
4',5-dihydroxy-6,7-(2,2-dimethylpyrano)-2'-methoxy-8-γ,γ-dimethylallylflavone



23: R = OH; 3'-Hydroxycycloartocarpin
24: R = H; Cycloartocarpin



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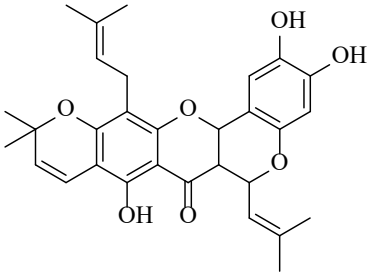
Chaplashin



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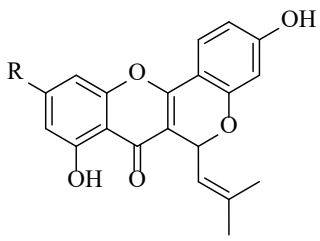
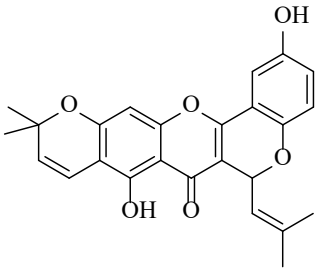
Cycloheterophyllin



27: R = OCH_3; Methoxycyclocommunol
28: R = OH; Cyclocommunol



29
Cudraflavone C

Supplementary Figure 2: Flavones isolated from Malaysia's *Artocarpus*

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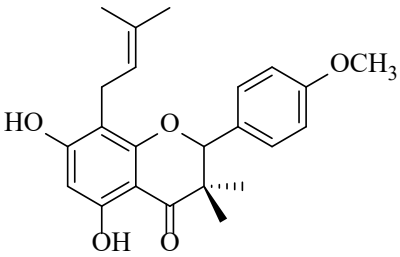
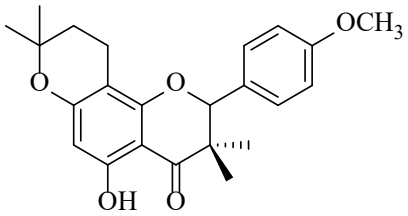


30

5,7-Dihydroxy-4'-methoxy-8-prenylflavanone



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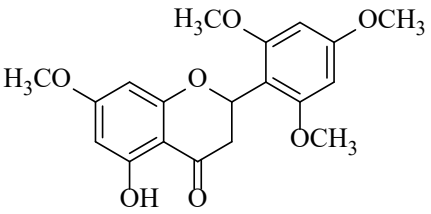
5-Hydroxy-7,8-(2,2-dimethyl-chromano)-4'-methoxyflavanone



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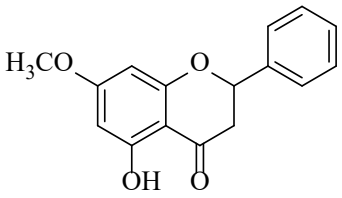
Heteroflavanone A



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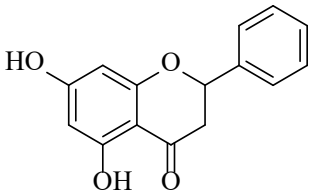
Pinostrobin



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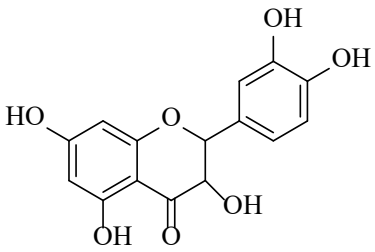
Pinocembrin



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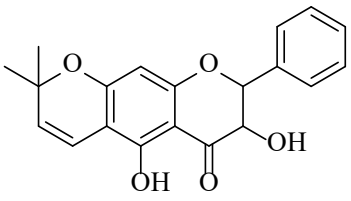
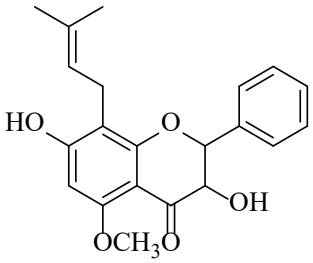
Catechin



36

Artoscortonol A



37

Artoscortonol B

Supplementary Figure 3: Flavanones and Flavanols isolated from Malaysia's *Artocarpus*

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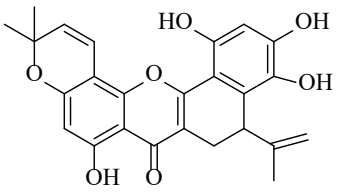

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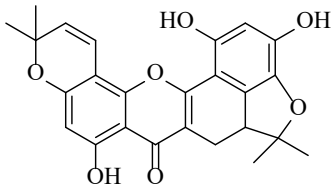
Artobiloxanthone



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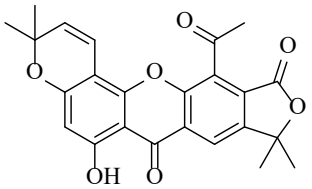
Cycloartobiloxanthone



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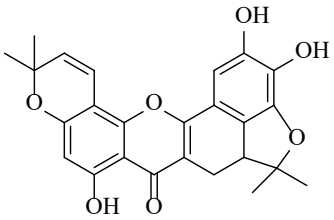
Artonol B



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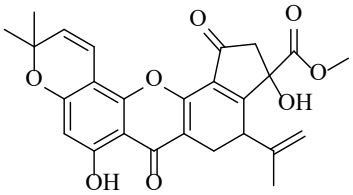
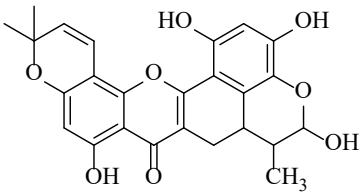
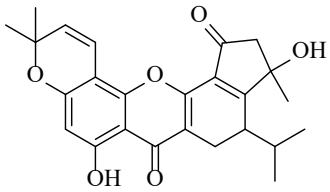
Artomandin



42
Artoindonesianin C



43
Pyranocycloartobiloxanthone A



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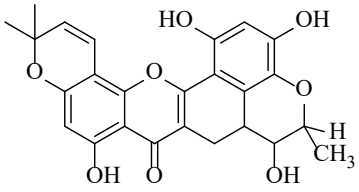
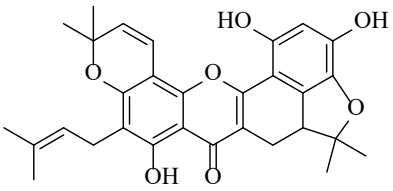
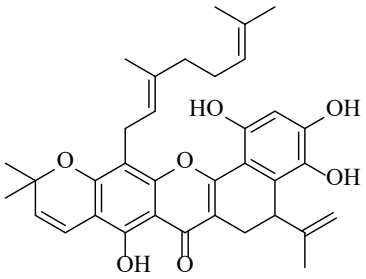
Dihydroartoindonesianin C



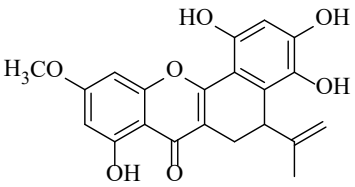
45
Pyranocycloartobiloxanthone B



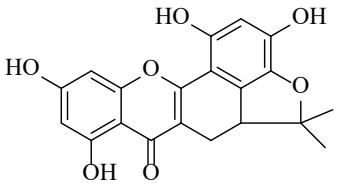
46
Artonin F



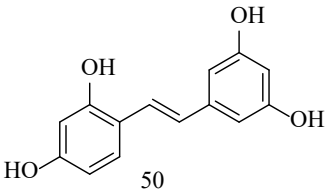
47
Artoindonesianin V



48
Elastixanthone



49
Artoindonesianin P



50
Oxyresveratrol

Supplementary Figure 4: Xanthones and Stilbenoid isolated from Malaysia's *Artocarpus*

Phytochemicals, Pharmacological and Ethnomedicinal Studies of *Artocarpus*: A Scoping Review

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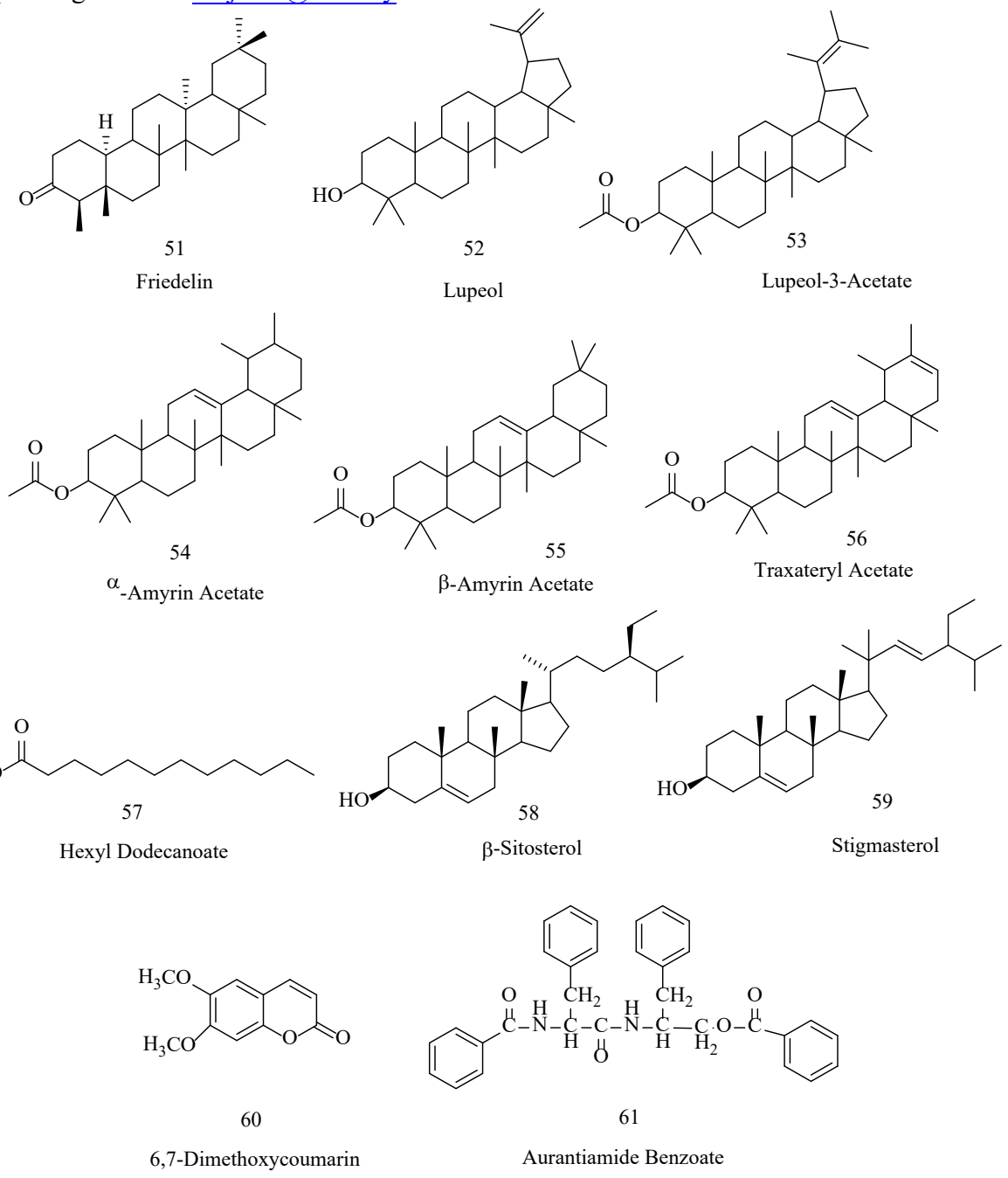

Supplementary Figure 5: Other secondary metabolites isolated from Malaysia's *Artocarpus*