***Review:***

# Phytochemistry and Biological Activities of *Amomum* Species

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***Abstract:*** Amomum *is a pungent and aromatic plant genus that contains 150–180 species, where Southeast Asia is the center of endemism, with Indonesia indigenous to 24 breeds. These species are used as spices and traditional medicine for the treatment of various diseases. This paper aims to provide* Amomum *species summarized data regarding phytochemistry and biological activities. Several studies have been carried out on the fruits, seeds, roots, rhizomes, and leaves of Amomum species from 1999 to 2024, as approximately 127 metabolites were isolated as flavonoid, diterpenoid, diarylheptanoid, monoterpenoid, sesquiterpenoid, phenylpropanoid, phenolic, and steroid groups. Besides cytotoxicity, anti-oxidant, and anti-inflammatory potentials; it also has an owed tendency for use as a chemical marker. The extracts and compounds obtained from the* Amomum *species were evaluated for biological activities, including cytotoxicity, anti-oxidant, anti-cancer, anti-proliferative, anti-inflammatory, anti-fungal, anti-microbial, neuroprotective, platelet anti-aggregation, and anti-diabetic properties. Tsaoko arilon (neolignane) had anti-proliferative and cytotoxic activity, with the highest reactions considered as lead compounds for further development. The findings highlighted the significance of using compounds from the* Amomum *genus in traditional medicine and the discovery of new medicines. Therefore, the results supported the concept of utilizing* Amomum *species as a potential source for producing biologically active compounds.*

***Keywords:*** Amomum*; biological activities; phytochemistry; Zingiberaceae*



## ■ INTRODUCTION

The Zingiberaceae family is one of the largest families in the plant kingdom, with 53 genera and over 1,200 species [1-2], These aromatic flowering plants are generally known as the ginger family and are widely distributed in the tropics and subtropics, with abundance specifically observed in Southeast Asia [2]. Approximately 19 genera and 375 species of this family are distributed in Indonesia [3]. Furthermore, the *Amomum* consists of 150 to 180 species and is found to be the second largest genus in the Zingiberaceae family [1,4]. The species of this genus are distributed all over Sri Lanka, through the Himalayas, China, Malaysia, and Northern Australia, with Southeast Asia serving as the center of endemism [4-5]. The characteristics of *Amomum* are identified as leafy branches with close-clasping sheaths, blades with a distinct plane of distich, and inflorescence growths on leafless shoots of the rhizome. In addition, several members of the ginger family have been widely employed as spices or flavoring agents based on their aromatic scents, as well as pungent and spicy tastes [2].

The phytochemical investigations of this genus have been previously reported, including the studies of several monoterpenoids, bicyclic nonanes, aldehydes, sesquiterpenoids, diterpenoids, diarylheptanoids, flavonoids, phenolic compounds, benzaldehydes, cyclopropanes, bicyclic aldehydes, steroids,

phenylpropanoids, and other chemical compounds [6-11]. Furthermore, the reported bioactivities of the isolated compounds from *Amomum* include anti-inflammatory, anti-obesity, anti-diabetic, anti-microbial, anti-quorum sensing, anti-microbial, cytotoxic, anti-bacterial, anti-oxidants, anti-tumor, and anti-cancer activities [8,11-20].

The rationale used as a search criterion in this study includes the phytochemical and biological activities published in PubMed, although Science Direct, Google Scholar, and Scifinder are also consulted. Since the search term *"Amomum"* is likely unclear for the inclusion of the plants, their traditional use, as well as ethnobotanical, ethnopharmacological, bioactivity, and phytochemistry properties, are also considered. Based on these conditions, further studies have been previously conducted over the last two decades, which subsequently identified as eight classes of metabolite, including diarylheptanoid as the main component. Monoterpenoid, sesquiterpenoid, diterpenoid, flavonoid, phenylpropanoid, as well as cycloterpenal, and benzaldehyde groups were also observed as chemical markers in these studies. The metabolites showed extensive biological activities based on cytotoxicity, anti-oxidant, anti-inflammatory, anti-fungal, anti-microbial, neuroprotective, platelet anti-aggregation, and anti-diabetic effects. Furthermore, Tsaoko arylon was observed as the strongest cytotoxic component, with promising characteristics for further development. According to several knowledges, the thorough evaluation of *Amomum* has not been published, therefore, necessitating the creation of a complete synopsis that includes the traditional uses, chemical content, and biological features of isolated compounds.

## ■ METHODOLOGY

The *Amomum* species was the subject of this investigation, which involved looking for literature on the subject. All synonym names were verified using plant databases, such as www.theplantlist.org and http://tropicos.org. This study reported the study on chemical and biological activities of the extracts, fractions, and isolated secondary metabolites of this plant species. Thus, this document summarizes the traditional uses and phytochemical and biological aspects of Amomum. All databases containing the keyword "Amomum" from search engines such as Scopus, Scifinder, PubMed, and Google Scholar were collected from 1999 to 2024. As a result, relevant papers were gathered. Additionally, *Amomum* species were categorized based on their ethnobotanical, ethnopharmacological, biological, and phytochemical characteristics. This study is helpful for further research on the future development prospects of plants and new drug discovery.

## ■ BOTANY

*Amomum* is the second biggest genus in the Zingiberaceae family [4-5], containing 150–180 species. The plant species of this genus are distributed all over Asia and Australia, with distribution centers observed in Southeast Asia [5]. Approximately 24 species are also found to be indigenous to Indonesia [5,21]. Furthermore, the plant species of *Amomum* are distributed in India, China, Korea, Japan, and Indonesia [8,22]. They are generally herbaceous plants and are found to inhabit wet forests, especially in small crevices and forest edges. Several species of this genus are also used as medicine, seasonings, and vegetables. Based on the morphological analysis of flowering material that originated at the type of site, the species belongs to Amomum genus [23-24]. The following are this herb's morphological characteristics: a pseudostem with a diameter of approximately 2.5 cm, slightly swollen and brownish at the base and yellowish-green at the apex; (a) 1.1–2.3 m tall; (b) a rhizome close to the soil surface; (c) a leafy shoot with 9–20 leaves per pseudostem; (d) glabrous, greenish-yellow leaf sheaths; (e) whole ligule, which is 7–9 mm long and has a ciliate edge, is tomentellous at the sheath junction, and is colored green and brown when it is young and completely grown; (f), approximately 0.5 cm long petiole is developing; (g) the lamina is linear to narrowly oblong, measuring 30–50 × 5–7 cm, green above and yellowish-green below, coriaceous, with a caudate apex and a rounded base. It is glabrous on both sides [25]. In a study by Bergman et al. [26], there was metabolic evidence that at least two different biosynthetic pathways of monoterpenes contribute to their volatility profile, namely, cyclic *p*-

menthanes, such as (-) isomenthone, and acyclic monoterpene alcohols, such as geraniol and (-)-citronellol derivatives (here citronelloid monoterpenes) [26].

## ■ PHYTOCHEMISTRY

Based on the reviewed literature from 1999 to 2024, a total of 127 compounds isolated from fruits, seeds, aerial parts, rhizome pieces, and roots of *Amomum* species originated from monoterpenoid, sesquiterpenoid, diterpenoid, flavonoid, diarylheptanoid (e.g. neolignan), benzaldehyde, cycloterpenaldehyde, phenylpropanoid, steroid, and other chemical groups. Furthermore, previous studies showed the distribution by a group of compounds (Fig. 1), which indicated that flavonoids (29.13%) were the largest metabolite with 37 compounds, diterpenoid (19.68%, 25 compounds) was the second, the third was diarylheptanoid (14.96%, 19 compounds) accompanied by monoterpenoids (14.96%, 19 compounds), sesquiterpenoids (9.45%, 12 compounds), other chemical groups (5.51%, 7 compounds), steroids (2.36%, 3 compounds), and benzaldehyde-cycloterpenal (2.36%, 3 compounds), and phenylpropanoid (1.57%, 2 compounds).

This overview of chemical contents and biological activity is in line with the findings of guide compounds from potential plants for drug development [27-28]. Amomum species are promising medicinal herbs and are commonly used by local people in traditional oriental medicine. Therefore, this plant is a potential source for therapeutic applications and potential drug development [29].

### Monoterpenoid

A total of 19 compounds were identified from 5 types of monoterpenoid since 2004, including monoterpene acyclic, monocyclic, glycosidic monoterpenoid, bicyclic monoterpene, and bicyclononane aldehyde [17,30-32]. The third-largest compound from this genus was monoterpenoid, as 9 acyclic compounds were isolated from *A. tsaoko* [30] (**1**–**9**). It could be a potential medicinal resource including essential oils [33]. Furthermore, Luo et al. [34] isolated two more monoterpene monocyclic from the fruit of *A. kravanh* (**10**–**11**). Besides that, Kim et al. [32] obtained two glycosidic monoterpenoids from the seeds of *A. xanthoides* (**12**–**13**). Monoterpenoid of *Amomum,* namely isotsaokoin **(14)** and tsaokoin **(15)**, as well as their oxygenated methylene derivatives were found in the fruits of *A. tsaoko* [17]. Besides tsaokoin [30] isolated two bicyclononane aldehyde compounds from *A. tsaoko*, namely (1*RS*, 5*SR*, 6*RS*)-5-hydroxybicyclo[4.3.0]non-2-en-2-carbaldehyde (**18**) and 6-hydroxyindane-4-carbaldehyde (**19**). The isotsaokoin-$CH_2OH$ (**16**) and tsaokoin-$CH_2OH$ (**17**) were further isolated as isomers of **14** and **15** from the *A. tsaoko.* The summary of the number and type of monoterpenoid compounds obtained from *Amomum* are shown in Table 1, while Fig. 2 shows the chemical structures of the constituents **1**–**19** [17].

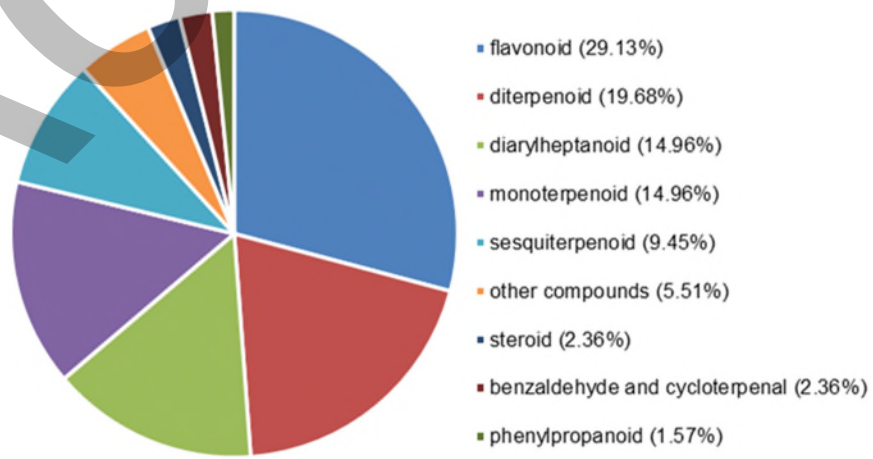



**Fig 1.** The distribution by a group of compounds from the *Amomum* species

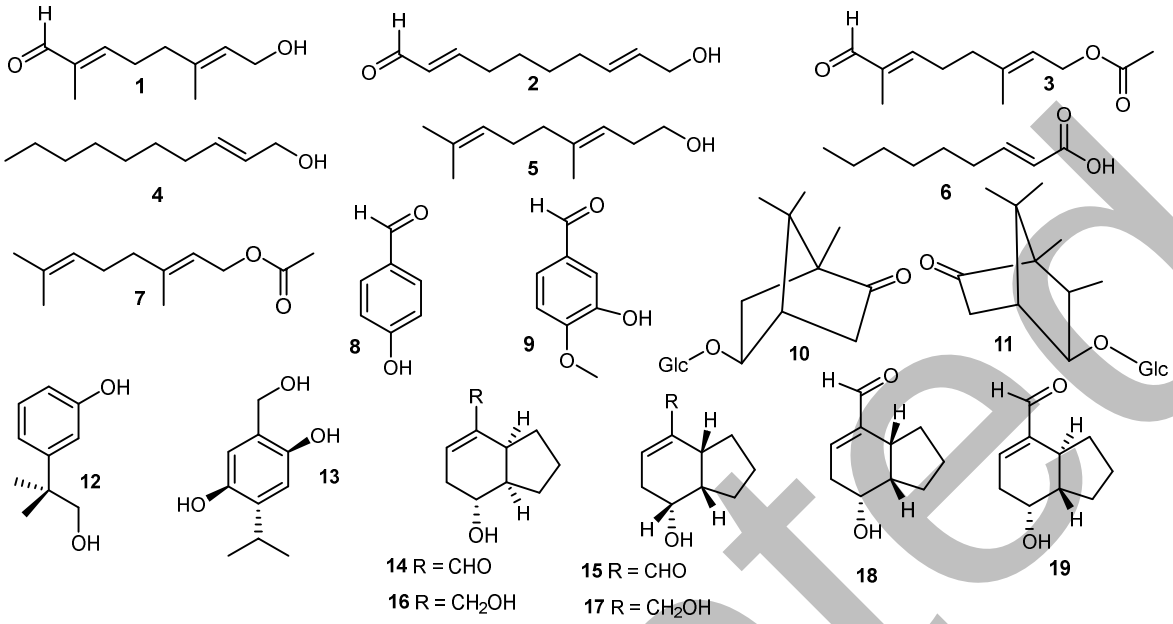



**Fig 2.** Monoterpenoid isolated from the Amomum genus

**Table 1.** Monoterpenoids from *Amomum* genus

| Type | Species | Compounds | Ref. |
|---|---|---|---|
| acyclic | *A. tsao-ko* | (*2E,6E*)-8-hydroxy-2,6-dimethyl-2,6-octadienal (**1**) | [30] |
| | | (2*E*,8*E*)-10-hydroxy-dexadienal (**2**) | |
| | | (2*E*,6*E*)-8-hydroxy-2,6-dimethyl-2,6-octadienal acetate (**3**) | |
| | | (2*E*)-decenol (**4**) | |
| | | geraniol (**5**) | |
| | | (2*E*)-decenal (**6**) | |
| | | geraniol acetate (**7**) | |
| monocyclic | *A. tsao-ko* | 4-hydroxy-benzaldehyde (**8**) | [30-31] |
| | | 4-methoxy-3-hydroxy-benzaldehyde (**9**) | |
| glycosidic monoterpene | *A. xanthioides* | (1*S*,4*S*,5*S*)-5-*exo*-hydroxy camphor 5-*O*-*β*-D-glucopyranoside (**10**) | [32] |
| | | (1*R*,4*R*,5*S*)-5-*endo*-hydroxy camphor 5-*O*-*β*-D-glucopyranoside (**11**) | |
| monocyclic | *A. kravanh* | (7*S*)-*p*-cymen-2,7,8-triol (**12**) | [34] |
| | | (3*R*,4*R*,6*S*) -*p*-men-1-en-3,6,10-triol (**13**) | |
| bicyclic | *A. tsaoko* | isotsaokoin (**14**) | [17] |
| | | tsaokoin (**15**) | |
| | | isotsaokoin $CH_2OH$ (**16**) | |
| | | tsaokoin $CH_2OH$ (**17**) | |
| | | tsaokoin (**15**) | [30] |
| bicyclononane aldehyde | *A. tsaoko* | (1*RS*,5*SR*,6*RS*)-5-hydroxy bicyclo[4.3.0]non-2-en-2-carbaldehyde (**18**) | [30] |
| | | 6-hydroxyindan-4-carbaldehyde (**19**) | |

## Sesquiterpenoid

The sesquiterpenoids are summarily demonstrated in Table 2, were characterized based on their structural skeleton, which are mainly divided into acyclic, bicyclic, and bergamotane types. Choi et al. [35] discovered nerodilol (**20**) from *A. xanthioides*, while hedychiol (**21**)

was isolated from the same species as pygmol (**22**) [31]. Chate and Nuntawong [10] obtained (**20**) from the air-dried powdered rhizomes of *A. uliginosum*. Spathulenol (**23**) and caryophyllene oxide (**24**) were also found in *A. xanthioides* [35]. Based on GC-MS identification, the main component of essential oil from the stems and leaves of this species in Vietnam were sesquiterpenoids [36]. A new bergamotane-type sesquiterpene named axanthiol A (**25**) was isolated from the rhizomes of *A. villosum* var *xanthioides*. Absolute configuration of **25** was confirmed by the Mosher ester method. Additionally, 6 known compounds were obtained (**26**–**31**) [37]. The known compounds (**30**, **31**) were also obtained from the fruits of *Elettaria cardamomum* Maton [38]. Their structures are shown in Fig. 3.

## Diterpenoids

A total of 25 diterpenes were isolated from the *Amomum* genus, including amoxanthoside (glycosides, **32**), a glycoside terpen from *A. xanthioides* [31]. Kim et al. [32] found amoxanthin A. (**33**). Moreover, isolated 4 novel diterpenoids with isospongian skeletons, kravanhin A-C (**34**–**36**), kravanhin D (**37**), and 3 new labdane-type were isolated from *A. kravanh* (**38**–**40**). The absolute configuration was determined by Snatzke's method with CD spectra and X-ray crystallography [39].

**Table 2.** Sesquiterpenoid of *Amomum* genus

| Type | Species | Compounds | Ref. |
|---|---|---|---|
| acyclic | *A. xanthioides,* | nerolidol (**20**) | [35] |
| | *A. uliginosum* | nerolidol (**20**) | [10] |
| | *A. xanthioies* | hedychiol A (**21**) | [31] |
| bicyclic | *A. xanthioides* | pygmol (**22**) | [31] |
| | *A. xanthioides* | spathulenol (**23**) | [35] |
| | | caryophyllene oxide (**24**) | [35] |
| Bergamotane | *A. villosum var* | axanthiol A (**25**) | [37] |
| monocyclic | *xanthioides* | 2$\beta$-5-isopentyl)-2$\beta$-methyl-5$\beta$-isopropenyl cyclohexanone (**26**) | |
| tricyclic | | isodrimenin (**27**) | |
| | | confertifolin (**28**) | |
| | | 8,8-dihydroxy-(13→17)-pentanorlabd-9(11)-en-12-oic acid 8a→12-lactone (**29**) | [37] |
| | *E. cardamomum* | elettarin B (**30**) | [37-38] |
| | | elettarin A (**31**) | [37-38] |

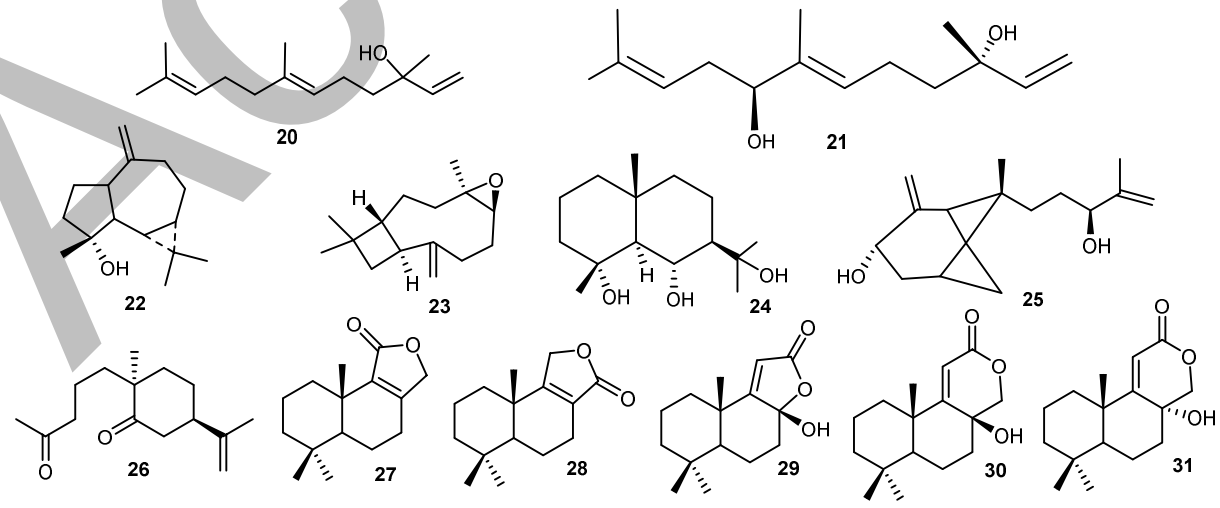



**Fig 3.** Sesquiterpenoid compound from the *Amomum* genus

Meanwhile, Yin et al. found 2 norditerpenoids with a 9-membered ring, amomaxins A-B (**41**–**42**) and isocoronarin D (**43**) from *A. maximum* [40]. Luo et al. found a rare labdane diterpene β-lactam, named amomax A (**44**), and 2 different labdane diterpenoids, amomax B-C (**45**–**46**), along with 2 known diterpenes, ottensinin (**47**), and (**38**) were isolated from the roots of *A. maximum* [41]. Afterward, based on the study of Chate and Nuntawong [10], isolated 4 diterpenes labdan from *A. uliginosum*, namely coronarine E (**48**), 16-hydroxylabdane-8 (**49**), 11,13-triene-15,16-olide (**50**), and vilosin (**51**). One diterpenoid compound found in *A. tsao-ko* is named coronadiene (**52**) [42].

There are interesting things related to terpenoids in the *Amomum* genus. Zhao et al. [43] found that the volatile terpenoids and transcriptomes of developing seeds of *A. villosum* and *A. longiligulare* were different. Both fruits of *A. villosum* and *A. longiligulare* used medicinally as *Amomi fructus* a famous traditional Chinese medicine. The results showed that the contents of bornyl acetate and borneol were higher in *A. villosum*. than *A. longiligulare*. It provides insight into the TPS-related molecular basis for the differences in biosynthesis and accumulation of bioactive terpenoids between *A. villosum* and *A. longiligulare* [43]. The second largest compounds of the genus are diterpenoids. One species that contains diterpenoid compounds was *A. maximum* [40]. *A. maximum* yielded 4 substantially rearranged labdane-type diterpenoids, maximumins A–D (**53**–**56**) [44]. The structures of these compounds in Table 3 are shown in Fig. 4.

## Flavonoid

The flavonoids from this genus were first reported

**Table 3.** Diterpenoid from the *Amomum* genus

| Type | Species | Compounds | Ref. |
|---|---|---|---|
| glycosides | *A. xanthioides* | amoxantoside A (**32**) | [31] |
| | | amoxanthin A (**33**) | [32] |
| isomerize isospongian | *A. kravanh* | kravanhin A (**34**) | [39] |
| | | kravanhin B (**35**) | |
| | | kravanhin C (**36**) | |
| | | kravanhin D (**37**) | |
| | | (12*Z*,14*R*)-labda-8(17),12-diene-14,15,16-triol (**38**) | |
| | | 3*β*,18-dihydroxylabda-8(17),13-dien-15,16-olide (**39**) | |
| | | (12*E*)-3*β*,18-dihydroxylabda-8(17),12-dien-16,15-olide (**40**) | |
| nor-labdan | *A. maximum* | amomaxin A (**41**) | [40] |
| | | amomaxin B (**42**) | |
| | | isocoronarin D (**43**) | |
| nor-labdan | *A. maximum* | amomax A (**44**) | [40] |
| | | amomax B (**45**) | |
| | | amomax C (**46**) | |
| | | ottensinin (**47**) | [39-41] |
| labdan | *A. uliginosum* | coronarine E (**48**), | [10] |
| | | 16-hydroxylabide-8 (**49**), | |
| | | 11,13-triene-15,16-olide (**50**) | |
| | | vilosin (**51**) | |
| trinorditerpene, | *A. tsaoko* | coronadiene (**52**) | [42] |
| rearrange labdan | *A. maksimum* | maximumin A (**53**) | [44] |
| | | maximumin B (**54**) | |
| | | maximumin C (**55**) | |
| | | maximumin D (**56**) | |

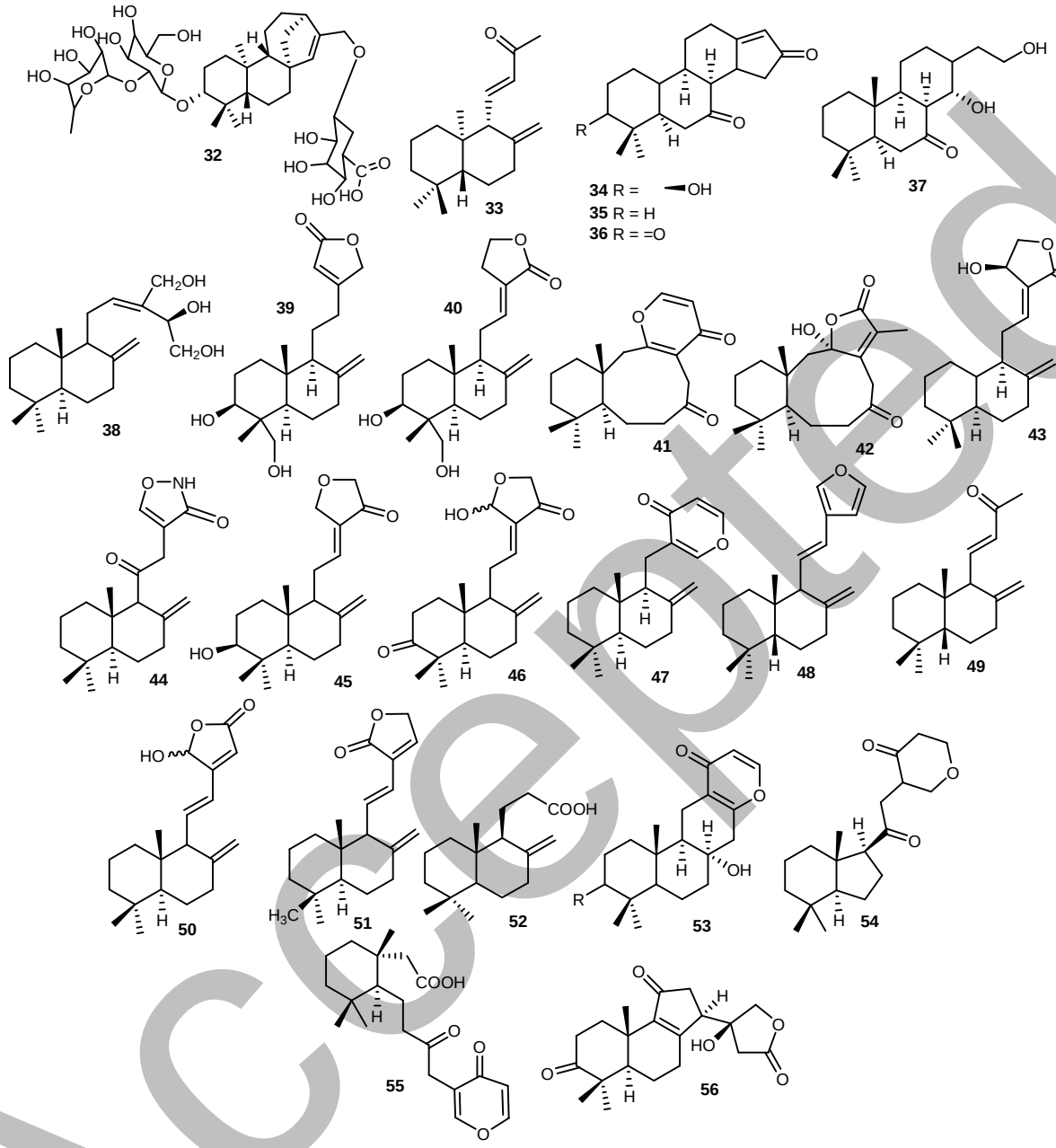



**Fig 4.** Chemical structures of the diterpenoid compounds from the *Amomum* genus

from *A. koenigii* by Dong et al. in 1999 as many as 11 compounds consisting of methylated kaempferol and methylated quercetin types (**57**–**67**) [45]. Afterward, 5 flavonoid compounds were isolated from the fruits of *A. tsaoko* for the first time [9], including 3 ordinary and 2 glycosidic flavonols. According to the study of Martin et al. isolated (+) epicatechin (**68**) and (-) catechin (**69**) for the first time from the fruits of *A. tsaoko* [6]. Meanwhile Zhang et al. [9] isolated (-) epicatechin (**68**) from similar fruit, with quercetin (**70**), quercetin-7-*O*-*β*-glucoside (**71**), and quercetin-3-*O*-*β*-glucoside (**72**) [9]. Then quercetin-3-rhamnopyranoside (**73**) was the flavonoid compound isolated from *A. xanthioides* [35].

Kim et al. [46] discovered 8 new compounds of geranylated and farnesylated pyranoflavanones (**74**–**81**) and 2 new farnesylated pyranochalcones (**82** and **83**) isolated from the methanol extract of *A. tsaoko* fruit. Then activity-guided isolation fractionation of MeOH

extract from dried fruit of *A. tsaoko* obtained 8 flavonoid compounds; alpinetin (**84**), naringenin-5-*O*-methyl ether (**85**), naringenin (**86**), hesperetin (**87**), 2',4',6'-trihydroxy-4-methoxy chalcone (**88**), and 2 other chalcone derivatives (**89**–**90**) [42]. Meanwhile, Dinata et al. [47] isolated for the first time from the roots of *A. compactum* methoxylated flavonoid compounds (**91**–**93**) [47]. A total of 37 flavonoid compounds have been isolated from the *Amomum* genus as the largest compounds from this genus (Table 4, Fig. 5).

## Diarylheptanoid

The third largest compounds from the *Amomum* were the diarylheptanoids, as 4 types were reportedly isolated from the 3 plant species of this genus. A total of nineteen diarylheptanoids were identified as hydroxyashabushiketol (**94**) from *A. xanthiodes* [31], hannokinol (**95**–**96**) from the fruits of *A. tsao-ko* [6-7], muricarpon (**97**–**104**) and muricarpin (**105**–**106**) from *A. muricarpum* [48-49]. Meanwhile, (5*S*)-5-hydroxy-1,7-bis(4-hydroxyphenyl)-heptane-3-one (**105**) was initially found with 5*R* type (**106**) in the plants. Furthermore, 2 new compounds with kravanhol A and B (**107** and **108**) and renealtin A (**109**) were isolated from *A. kravanh* [50], as their AC were determined by Mosher's method and CD experiments [39]. Neolignane (**111**) was also obtained from *A. tsao-ko* [7], while Yang et al. [30]

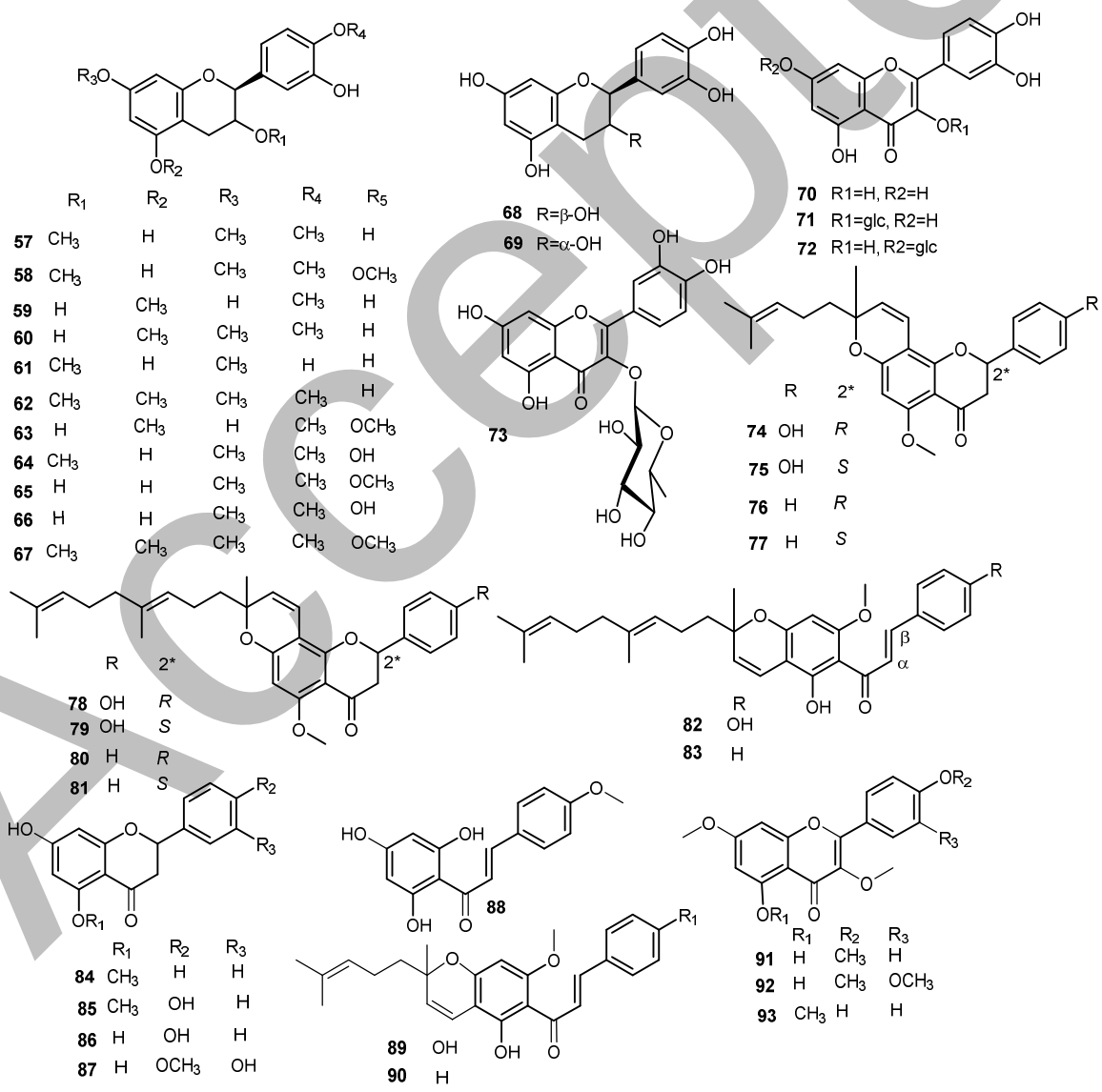



**Fig 5.** Chemical structures of flavonoid compounds from *Amomum* genus

**Table 4.** Flavonoid from the *Amomum* genus

| Type | Species | Compound | Ref. |
|---|---|---|---|
| methylated kaempferol | *A. koenigii* | 5-hydroxy-3,7,4'-trimethoxyflavone (**57**) | [45] |
| | | 5-hydroxy-3,7,3′,4′-tetramethoxyflavone (**58**) | |
| | | 3,7-dihydroxy-5,4′-dimethoxyflavone (**59**) | |
| methylated quercetin | | 3-hydroxy-5,7,4'-trimethoxyflavone (**60**) | |
| | | 5,4′-dihydroxy-3,7-dimethoxyflavone (**61**) | |
| | | 3,5,7,4′-tetramethoxyflavone (**62**) | |
| | | 3,7-dihydroxy-5,3′,4′-trimethoxyflavone (**63**) | |
| | | 5,3′-dihydroxy-3,7,4'-trimethoxyflavone (**64**) | |
| | | 3,5-dihydroxy-7,3′,4′-trimethoxyflavone (**65**) | |
| | | 3,5,3'-trihydroxy-7,4′-dimethoxyflavone (**66**) | |
| | | 3,5,7,3′,4′-pentamethoxyflavone (**67**) | |
| hydroxylated quercetin | *A. tsao-ko* | (-) epicatechin (**68**) | [6,9] |
| | | catechin (**69**) | [6,9] |
| flavonol | *A. tsao-ko* | quercetin (**70**) | [9] |
| glycosidic flavonol | *A. tsao-ko* | quercetin-7-*O*-*β*-glucoside (**71**) | [9] |
| | | quercetin-3-*O*-*β*-glucoside (**72**) | |
| glycosidic flavonol | *A. xanthioides* | quercetin-3-rhamnopyranoside (**73**) | [35] |
| pyranoflavanones | *A. tsao-ko* | tsaokonol A (*R*) (**74**) | [46] |
| | | tsaokonol B(*S*) (**75**) | |
| | | tsaokonol C(*R*) (**76**) | |
| | | tsaokonol D(*S*) (**77**) | |
| farnesylated pyranoflavanones | *A. tsao-ko* | tsaokonol E (*R*) (**78**), | [46] |
| | | tsaokonol F (*S*)(**79**) | |
| | | tsaokonol G (*R*) (**80**) | |
| | | tsaokonol H (*S*) (**81**) | [46] |
| | *A. tsao-ko* | tsaokonol I (**82**) | |
| | | tsaokonol J (**83**) | |
| flavanones | *A. tsao-ko* | Alpinetin (**84**) | [42] |
| | | naringenin-5-*O*-methyl ether (**85**) | [42] |
| | | naringenin (**86**) | |
| | | hesperetin (**87**) | |
| chalcone | | 2',4',6'-trihydroxy-4-methoxy chalcone (**88**) | [42] |
| pyranochalcone | | 4-hydroxyboesenbergin B (**89**) | |
| | | boesenbergin B (**90**) | |
| methoxylated kaempferol | *A.compactum* | 5-hydroxy-3,7,4`-trimethoxy kaempferol (**91**) | [47] |
| | | 5-hydroxy-3,7,3',4'-tetra methoxy kaempferol (**92**) | |
| | | 4'-hydroxy-3,5,7-trimethoxy kaempferol (**93**) | |

isolated tsaokoarylon (**112**) from the dried fruits. These compounds are shown in Table 5 and Fig. 6.

### Benzaldehyde and Cycloterpenal

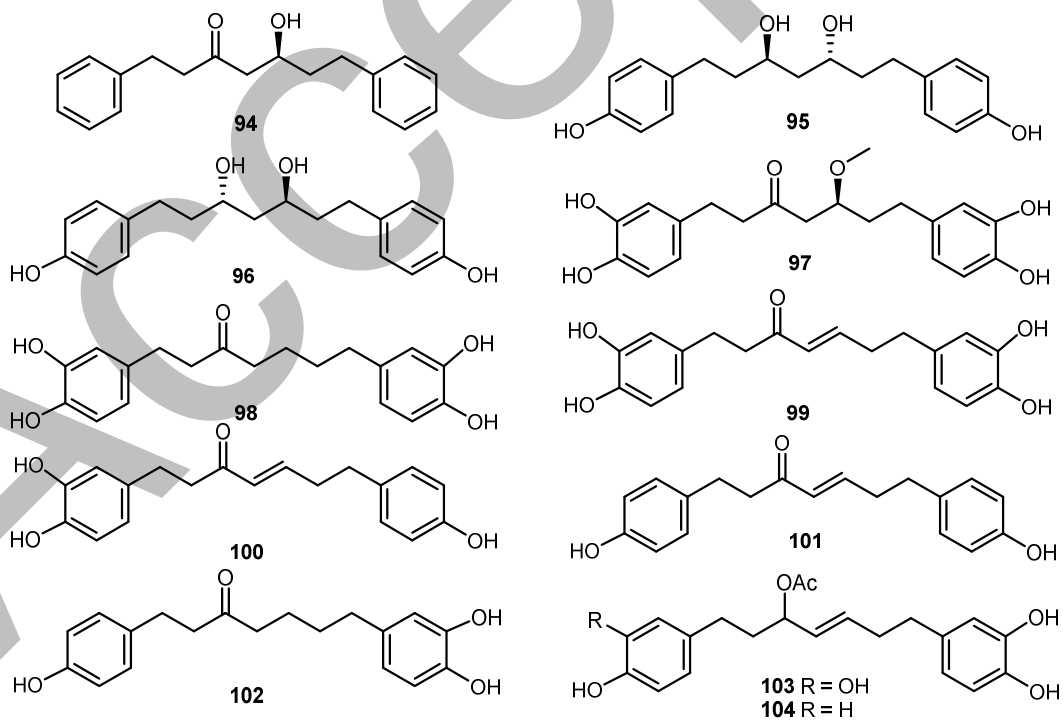
There were only 3 compounds in this chemical group from the *Amomum* genus. Hong et al. [8] reported the isolation of amotsaokonal A (**113**), as well as the B and C types (**114** and **115**) from the ethanol extract of *A. tsaoko* fruit (Fig. 7, Table 6).

### Phenylpropanoid

Chai et al. [11] reported the isolation of 2 phenyl

**Table 5.** Diarylheptanoid compounds from the *Amomum* genus

| Type | Species | Compounds | Ref. |
|---|---|---|---|
| dihydroketol | *A. xanthoides* | hydroxyashabushiketol (**94**) | [31] |
| hannokinol | *A. tsao-ko* | hannokinol (**95**) | [6] |
| | | *meso*-hannokinol (**96**) | [7] |
| muricarpon | *A. muricarpum* | muricarpon A (**97**) | [48] |
| | | muricarpon B (**98**) | |
| | | 1,7-di-(3',4'-dihydroxyphenyl)-4-hepten-3-one (**99**) | |
| | | 1-(3',4'-dihydroxyphenyl)-7-(4"-hydroxyphenyl)-4-hepten-3-one (**100**) | |
| | | 1,7-bis(*p*-hydroxyl)-4-hepten-3-on (**101**) | |
| | | muricarpin (**102**) | |
| | | 1,7-bis(3,4-dihydroxyphenyl)-heptane-3-yl acetate (**103**) | |
| | | 1-(4'-hydroxyphenyl)-7-(3",4"-dihydroxyiphenyl)-heptane-3-yl acetate (**104**) | |
| muricarpin | *A. muricarpum* | (5*S*)-5-hydroxy-1,7-*bis*(4-hydroxyphenyl)-heptane-3-*on* (**105**) | [49] |
| | | (5*R*)-5-hydroxy-1,7-*bis*(4-hydroxyphenyl)-heptane-3-*on* (**106**) | |
| kravanhol | *A. kravanh* | kravanhol A (**107**) | [50] |
| | | kravanhol B (**108**) | |
| | | renealtin A (**109**) | |
| neolignane | *A. tsao-ko* | 2,3-dihydro-2-(4'-phenyl hydroxy)-6-[(3,4"-hydroxy-5"-methoxy) phenyl]-4-pyron (**110**) | [7] |
| | | 4-dihydro-2-(4'-hydroxy-phenylmethyl)-6-[(3",4"-dihydroxy-5" methoxyphenyl) methylene]-pyran-3,5-dion (**111**) | [7] |
| | | tsaokoarylon (**112**) | [30] |



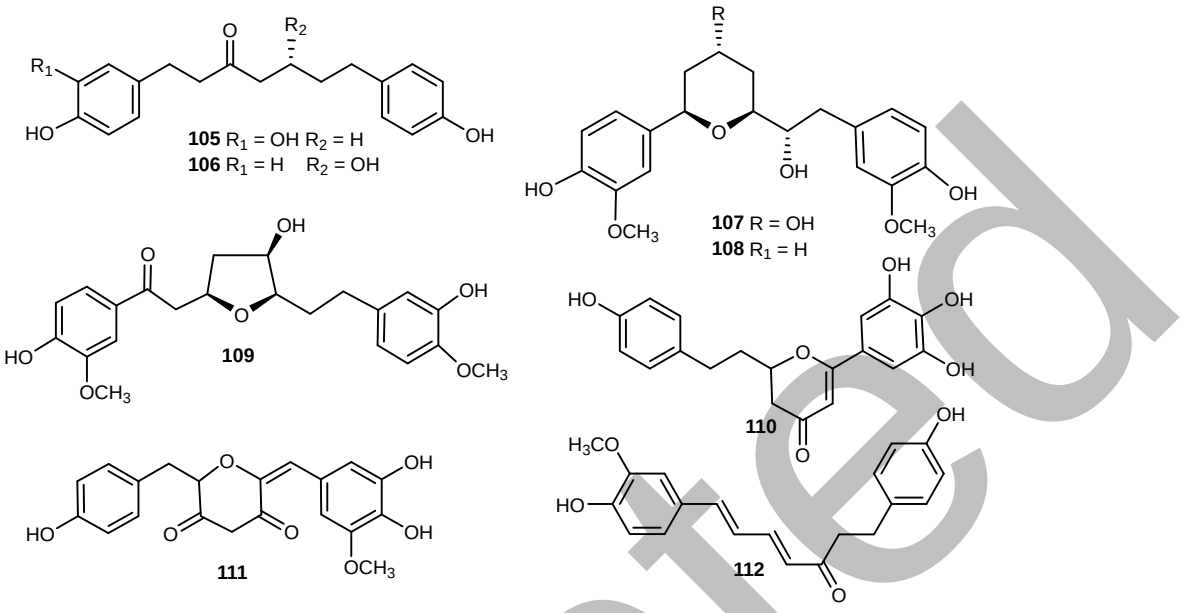



**Fig 6.** Chemical structures of diarylheptanoid compounds from the *Amomum* genus

**Table 6.** Benzaldehyde-cycloterpenal, phenylpropanoid, steroid, and other chemical groups of the *Amomum* genus

| Type | | Species | Compound | Ref. |
|---|---|---|---|---|
| benzaldehyde | | *A. tsao-ko* | amotsaokonal A (**113**) | [8] |
| cycloterpenal | | *A. tsao-ko* | amotsaokonal B (**114**) | |
| | | | amotsaokonal C (**115**) | |
| phenylpropanoids | | *A. paratsao* | *trans*-(decyl-2-*en*)-3-(4-hydroxy-3-methoxy-phenyl) propenoate (**116**) | [11] |
| | | | *trans*-10-hydroxydecyl-3-(4-hydroxyl) propenoate (**117**) | |
| steroid | *β*-sitosterol | *A. tsao-ko* | *β*-sitosterol (**118**) | [6] |
| | *β*-sitosterol glycoside | | *β*-sitosterol-3-*O*-glucoside (**119**) | |
| | stigmastan | *A. uliginosum* | stigmast-4-*en*-3-on (**120**) | [10] |
| other | ester/fatty acids | *A. tsaoko* | methyl linolenate (**121**) | [8] |
| | | | *trans*-nerolidol (**122**) | |
| | | | (2*E*)-dodecenyl acetate (**123**) | |
| | | | acid (*E*)-des-2-enoic (**124**) | |
| | | | pyrrol-2-carboxylic acid (**125**) | |
| | | | catechol (**126**) | |
| | | | myrciaphenone A (**127**) | |

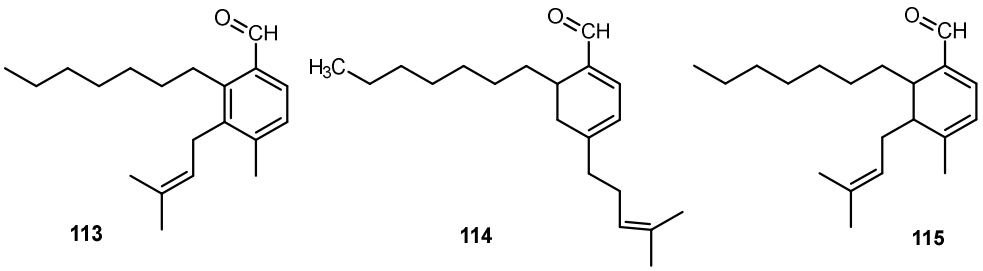



**Fig 7.** Chemical structures of benzaldehyde and cycloterpenal compounds from *A. tsaoko*

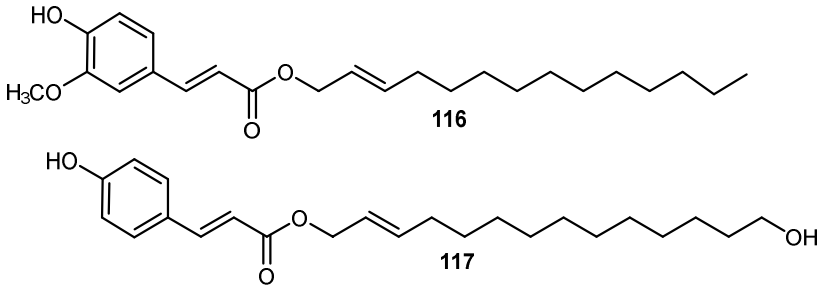



**Fig 8.** Chemical structure of phenylpropanoid compounds from the *Amomum* genus

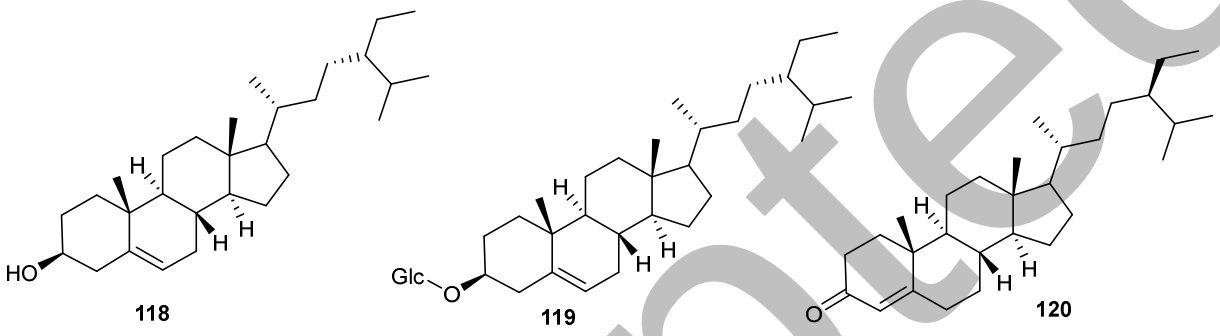



**Fig 9.** Chemical structure of steroid compounds from the *Amomum* genus

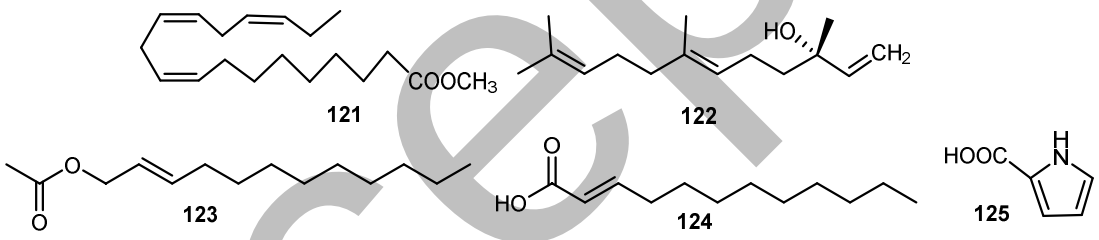



**Fig 10.** Chemical structure of other chemical groups compounds from the *Amomum* genus

propanoids from the methanol extracts of *A. paratsao* fruits. This included *trans*-(decyl-2-en)-3-(4-hydroxy-3-methoxy-phenyl)propenoate (**116**) and *trans*-10-hydroxdecyl-3-(4-hydroxyphenyl)propenoate (**117**) [11]. The chemical structure is shown in Fig. 8, whereas the summary of compounds is shown in Table 6.

## Steroid and Other Chemical Groups

Three types of steroid compounds such as b-sitosterol (**118**), β-sitosterol-3-*O*-glucoside (**119**), and stigmast-4-en-3-on (**120**), were isolated from the fruits of *A. tsao-ko* [8] and rhizome of *A. uliginosum* (J. Koenig) [10]. Other chemical groups included methyl linolenate (**121**), *trans*-nerolidol (**122**), (2*E*)-dodecenyl acetate (**123**), acid (*E*)-des-2-enoic (**124**), and pyrrole-2-carboxylic acid (**87**), obtained from the fruits of *A. tsao-ko*. The chemical structure of compounds **118**–**120** was shown in Fig. 9, whereas compounds **121**–**125** and **126**–**127** were shown in Fig. 10 and 11, respectively. In addition, the summary of compounds is shown in Table 6.

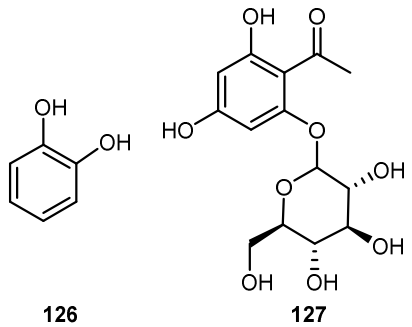



**Fig 11.** Structure of catechol and myrciaphenone A from *Amomum* genus

## ■ ETHNOBOTANY AND MEDICAL USES

Based on drug discovery and development, there was an urgent need to explore effective and less toxic alternative sources. The approach of the ethnobotanical study and traditional medical uses played an important role due to the effectiveness of drugs. The study of how local people interact with their natural surroundings, particularly how they use plants for internal purposes, is known as ethnobotany [3]. According to the literature, various *Amomum* species have long been utilized in Asian medicine to treat various ailments. As one of the most studied spices, *A. cardamomum* is utilized as a medicine in Indonesia for several illnesses, including gallstones, TB, renal disease, mouth and throat infections [51]. This kind of ginger was also employed as a tonic in cookery, thanks to its rhizome and leaves [52]. Additionally, *A. compactum* was utilized by Indonesians for a variety of reasons, including aromatherapy, traditional medicine, health beverages, and spice cookery [21]. Cardamom (*A. compactum*) was used in traditional Chinese medicine as a cancer treatment. In principle, plants used as an anti-cancer compound inhibited cleavage cells. *A. repoense* Pierre ex Gagnep plant also had multiple medicinal uses in Vietnam, which ranged from appetite stimulants to pain relievers and diarrhea [20]. The fruit of *A. kravanh* Pierre ex Gagnep was often used to treat stomach diseases and digestive disorders [34]. In Southern China, Vietnam, Thailand, and Cambodia, this fruit is well renowned. The volatile oil found in *A. compactum* seeds is used in India to flavor bread, cakes, curries, coffee, and confections. It was also used to treat a various neurological, cardiovascular, and gastrointestinal conditions [52]. *A. subulatum* Roxb. fruit is an old and famous spice; used as a flavoring agent for various native Eastern Himalayas dishes, especially in Nepal, Bhutan, and India [52]. *A. tsao-ko* Crevost et Lemarie has long been used in China and Korea to treat inflammatory, diarrhea, malaria, throat infections, and abdominal pain [8,53].

## ■ BIOLOGICAL ACTIVITIES

Several parts of the *Amomum* plant were used as a traditional treatment for various diseases in different countries, e.g., the black cardamom (*A. tsao-ko* Crevost et Lemarié). For instance, this herb's separated epicatechin (**68**) and tsaokoin (**15**) prevented BV2 microglial cells from producing NO when exposed to LPS [54]. *A. compactum* utilized as a flavor in Asia, have anti-oxidant properties for their ability to scavenge radicals [55]. Furthermore, several studies have demonstrated the anti-fungal, anti-microbial, cytotoxic, apoptotic, and anti-oxidants activities [17,19,21,33]. *A. tsao-ko* contains anti-tumor, anti-oxidant, cytotoxic, anti-proliferative, and anti-inflammatory components [8-9,56]. By inducing NRF2/HO-1 in LPS-induced RAW 264.7 macrophages, it was discovered that the ethanol extract of *A. tsaoko* fruit also had anti-inflammatory properties [57]. The seeds of the ethanol extracts inhibited spingosine kinases 1 and 2 (SPHK ½) [58]. Additionally, 2 phenolic compounds, a fatty acid, and a sesquiterpene alcohol from *A. tsao-ko* showed the assessment of anti-diabetic efficacy by oil red O staining in 3T3-L1 cells [13]. The studies inform the therapeutic potential of *A. subulatum* and *A. xanthioides*. The data indicate that extracts of both species possess high biological activity, enhancing their potential value in various therapeutic applications [43]. The evaluated parts of the *Amomum* plants included the seeds, roots, essential oils, and fruits, which specifically obtained the most attention [8,11,15,34]. Various biological activities also interestingly showed anti-inflammatory, anti-oxidant, anti-tumor, anti-bacterial, anti-microbial, platelets anti-aggregation, anti-diabetic, and cytotoxic reactions [57-59]. Tables 7 and 8 display the bioactivity of the *Amomum* species based on the plant parts and phytochemical ingredients, respectively.

### Cytotoxicity

Six various cytotoxic compounds were isolated from Amomum species, including tsaokoarylon (**112**) and geraniol (**5**) from the fruits of *A. tsao-ko* [30]. Compound **5**, (1*S*,4*R*,5*S*)-(+)-5-endo-hydroxycamphor (**10**), (1*R*,4*R*,5*S*)-5-endo-hydroxycamphor 5-*O*-b-D-glucopyranoside (**12**), and amoksantoside A (**22**), were obtained from *A. xanthoides* [17,31]. The **112** had anti-proliferative and cytotoxic activities, which had the highest $IC_{50}$ value of 46 µM against murine neuroblastoma (N2a) cells [10]. Additionally, through a

**Table 7.** Biological activity based on plant parts of the *Amomum* genus

| Species | Plant parts | Bioactivity | Ref. |
|---|---|---|---|
| *A. tsao-ko* | seed | anti-inflammatory, anti-proliferative, | [57] |
| | | anti-oxidative, neuroprotective | [57] |
| | fruit | anti-fungal | [17] |
| | | anti-microbial, | [30] |
| | | anti-inflammatory, | [8] |
| | | neuroprotective | [9,57] |
| | | anti-oxidant and anti-tumor | [7,9] |
| | | anti-obesity, anti-diabetic | [13,59] |
| | | cytotoxic | [9] |
| | essential oil | anti-quorum sensing, | [14] |
| | | anti-bacterial | [14,73] |
| | | anti-microbial | [71] |
| *A. kravanh* | fruit | platelet anti-aggregation | [34] |
| *A. paratsao* | fruit | anti-inflammatory | [11] |
| *A. subulatum* | seed | antioxidant | [60] |
| | | anti-microbial | [60] |
| *A. xanthoides* | root | cytotoxic | [32] |
| *A. dealbatum* | fruit | anti-bacterial | [62] |

**Table 8.** Biological activity of phytochemical constituents from the *Amomum* genus

| No | Biological activity | Compounds or extracts | Species | Ref. |
|---|---|---|---|---|
| 1. | Cytotoxicity | tsaokoarylon (**112**) | *A. tsao-ko* | [30] |
| | | (1*S*,4*R*,5*S*)-(+)-5-*endo*-hydroxy camphor (**10**) | *A. xanthoides* | [31] |
| | | geraniol (**5**) | | |
| | | geraniol (**5**) | *A. tsao-ko* | [30] |
| | | (1*R*,4*R*,5*S*)-5-*endo*-hydroxy camphor,5-*O*-*β*-D-glucopyranoside (**12**) | *A. xanthoides* | [32] |
| | | amoksantoside A (**22**) | *A. tsaoko* | [17,31] |
| | | hydroxyashabushiketol (**94**) | | [31] |
| 2. | Anti-oxidant | (+)-epicatechin (**68**) | *A. tsao-ko* | [6,7] |
| | | (-)-catechin (**69**) | | [6] |
| | | hannokinol (**95**) | | [6,9] |
| | | *meso*-hannokinol (**96**) | | [6] |
| | | quercetin (**70**) | *A. tsao-ko* | [7] |
| | | quercetin-3-*O*-glucoside (**71**) | | |
| | | quercetin-7-*O*-glucoside (**72**) | | |
| | | 2,3-dihydro-2-(4'-phenylhydroxy)-6-[3,4"-ddihydroxy5"-methoxy) phenyl]-4-pyron (**67**) | *A. tsao-ko* | [9] |
| | | 4-dihydro-2-(4′-hydroxy-phenylmethyl)-6-[(3″,4″-dihydroxy-5″-methoxyphenyl)methylene]-pyran-3,5-dion (**68**) | | |
| | | water extracts and methanol extracts | *A. cardamomum* | [59] |
| 3. | Anti-cancer | cardamom oil | *A. cardamomum* | [66] |
| | | acetone extracts | | [68] |
| | | zerumbon (essential oil) | *A. repoense* | [12] |
| 4. | Anti-proliferative | zerumbon (essential oil) | *A. gagnepainii* | [12] |

| No | Biological activity | Compounds or extracts | Species | Ref. |
|---|---|---|---|---|
| | | tsaokoin (**15**) | *A. tsao-ko* | [30] |
| | | (2*E*,6*E*)-8-hydroxy-2,6-dimethyl-2,6-octadienal (**1**), | | |
| | | tsaokoarylone (**112**) | | |
| | | (2*E*,8*E*)-10-hydroxy-decadienal (**2**) | | |
| | | (1*RS*,5*SR*,6*RS*)-5-hydroxy bicyclo[4.3.0]non-2-en-2-carbaldehyde (**18**) | | |
| | | 6-hydroxyindan-4-carbaldehyde (**19**) | | |
| 5. | Anti-inflammatory | amomaxin A (**41**) | *A. maximum* | [40] |
| | | amomaxin B (**42**) | | |
| | | kravanhol A (**107**) | | [50] |
| | | kravanhol B (**108**) | | |
| | | renealtin (**109**) | | |
| | | ethanol extract | *A. tsao-ko* | [57] |
| | | (+) epicatechin (**68**) | *A. tsao-ko* | [7] |
| | | (-)-catechin (**69**) | | |
| | | quercetin (**70**) | | |
| | | quercetin 3-*O*-glucoside (**71**) | | |
| | | quercetin-7-*O*-glucoside (**72**) | | |
| | | *messo*-hannokinol (**96**) | | [6] |
| | | amotsaokonal A (**113**) | | [8] |
| | | amotsaokonal B (**114**) | | |
| | | amotsaokonal C (**115**) | | |
| | | methyl linolenate (**121**) | | |
| | | *trans*-nerolidol (**122**) | | |
| | | (2*E*)-dodecenyl acetate (**55**) | *A. gagnepainii* | [12] |
| | | (*E*)-des-2-enoat acid (**56**) | *A. paratsao* | [11] |
| | | pyrrol-2-carboxylic acid (**57**) | | |
| | | β-caryophyllene | | |
| | | *trans*-(decyl-2-ene)-3-(4-hydroxy-3-methoxy-phenyl)propenoate (**47**) | | [11] |
| | | *trans*-10-hydroxyethyl-3-(4-hydroxyphenyl) propenoate (**48**) | | [11] |
| | | essential oils | *A. subulatum* | [70] |
| 6. | Anti-fungal | isotsaokoin (**14**) | *A. tsao-ko* | [17] |
| | | tsaokoin (**15**) | | [30] |
| | | isotsaokoin $CH_2OH$ (**16**) | | |
| | | tsaokoin $CH_2OH$ (**17**) | | [30] |
| 7. | Anti-microbial | geranial | | |
| | | geraniol (**5**) | *A. tsao-ko* | [30] |
| | | essential oil | *A. tsao-ko* | [71] |
| 8. | Neuroprotective | quercetin (**70**) | *A. tsao-ko* | [7] |
| | | quercetin 3-*O*-glucoside (**71**) | | |
| | | quercetin-7-*O*-glucoside (**72**) | | |
| 9. | Platelet anti-aggregation | (7*S*)-*p*-simen-2,7,8-triol (**12**) | *A. kravanh* | [34] |
| | | (3*R*,4*R*,6*S*)-*p*-men-1-*en*-3,6,10-triol (**13**) | | |
| 10. | Anti-diabetic | water extracts and methanol extracts | *A. cardamomum* | [59] |
| | | methyl linolenate (**121**) | | |

| No | Biological activity | Compounds or extracts | Species | Ref. |
|---|---|---|---|---|
| | | *trans*-nerolidol (**122**) | *A. tsao-ko* | [13] |
| | | catechol (**126**) | | |
| | | phloroacetophenone | | |
| | | 2′-*O*-glucoside myrciaphenone A (**127**) | | |

mechanism connected to apoptosis, **5** and 1,8-cineol (an essential oil from *A. tsao-ko*) demonstrated cytotoxicity to various cell types and induced cytotoxic activities in liver cancer cells (HepG2) [30]. Based on the *in vitro* sulforhodamin B (SRB) assay, the cytotoxicity of compounds **10**, **12**, **23**, and **36** against A549, SK-OV-3, SK-MEL-2, and HCT15 showed that hydroxyashabushiketol (**94**) was the highest active compound against skin melanoma (SK-MEL-2), with the $IC_{50}$ value of 11.73 mM. However, other derivatives showed low cytotoxicity, such as glycosylated compounds ($IC_{50}$ > 100 mM). Kim et al. [32] reported compounds from *A. xanthoides* seeds based on 2 new monoterpene glycosides, namely **12** and (1*R*,4*R*,5*S*)-5-endo-hydroxycamphor-5-*O*-*β*-D-glucopyranoside (**13**) (Fig. 2). Meanwhile, the cytotoxic activities were above 100 nM against lung (A-549), ovarian (SK-OV-3), melanoma skin (SK-MEL-2), and colon (HCT15) cancer cells, respectively. Yang et al. [33] identified the chemical components of 73 essential oil compounds from the *A. tsaoko* fruit and tested their cytotoxic activities. The, 1,8-cineol was the highest component of essential oil (45%), providing the strongest cytotoxic and apoptotic activities against HepG2, with an $IC_{50}$ of 2.81 μg/mL. While, geraniol gave a value of 214.9 μg/mL.

## Anti-oxidant

Martin et al. [6], isolated 2 flavonoids and diarylheptanoids from the fruits of *A. tsao-ko*, namely (+)-epicatechin (**68**) and (-)-catechin (**69**), as well as (+)-hannokinol (**95**) and *meso*-hannokinol (**96**), respectively. Using colorimetric electron spin resonance (ESR) and 1,1-diphenyl-2-picrylhydrazyl (DPPH) studies, the radical scavenging ability of these compounds was assessed. The **95** showed the highest activity at the $IC_{50}$ value of 4.79 mM, while **68** and **69** produced 5.15 mM. This activity was supported by Yang et al. [33] and Zhang et al. [7], which isolated **68** and **95** from similar plant species, respectively. Zhang et al. [7] also isolated 2 compounds, namely 2,3-dihydro-2-(4′-hydroxy-phenylmethyl)-6-[(3″,4″-dihydroxy-5″-methoxy) phenyl]-4-pyrone (**48**) and 4-dihydro-2-(4′-hydroxy-phenylmethyl)-6-[(3″,4″-dihydroxy-5″-methoxyphenyl) methylene]-pyran-3,5-dione (**49**). Furthermore, 2 new compounds were found to exhibit higher anti-oxidant activities, with inhibitory concentrations of 79% and 83% at 80 mg/mL. Numerous investigations have continuously demonstrated a reasonable relationship between the structures of phenolic compounds such as side chain design and substitutions on aromatic rings and their anti-oxidant activity [60-61]. This was also observed to be the cause of phenolic hydroxyl groups to have anti-oxidant and anti-diabetic effects. [61-63]. Zhang et al. [7], reported the isolation of flavonoids from the ethyl acetate fraction. With $H_2O_2$-induced PC-12 cells, quercetin (**70**) exhibited the highest neuroprotective effect and 78.9% cellular viability at 50 mg/mL. Additionally, at a dosage of 100 mg/mL, it demonstrated strong DPPH radical scavenging activity (> 80%). The flavonoids could suppress oxidative processes linked to anti-cancer and anti-diabetic activities [64-77]. This is also revealed role of free radical in human inflammatory diseases [65]. Based on the DPPH and FRAP methods, the $IC_{50}$ data of water and methanol extracts were 11.04 and 10.59 mM, respectively, when compared to the antioxidant activity [59].

## Anti-cancer and Anti-proliferative

The plant *A. compactum*, commonly referred to as cardamom, may include anti-cancer substances. However, traditional Chinese medicine first documented the use of cardamom as a cancer treatment in Deng et al. [20]. Biswas et al. [64] and Srinivasan [66] showed that 10 μL oil of *A. compactum* against experimental animals actively influenced metabolism enzymes to prevent cancer. Cardamom seed (*A.*

*compactum*) extract potentially use as anti-cancer and anti-bacterial [68]. Additionally, cardamom has anti-inflammatory, anti-proliferative, and proapoptotic properties that help to lessen colon cancer caused by azoxymethane [67]. Furthermore, 10 µL of cardamom oil daily for 2 weeks beneficially affected the enzymes involved in xenobiotic metabolism, which is likely to prevent cancer [69]. Huong et al. [12] identified the presence of α-pinene, β-pinene, E-β-ocimene γ-terpinene, β-caryophyllene, and zerumbone compounds from *A. gegnapainii* and *A. repoense* in Vietnam. β-caryophyllene and zerumbone were also previously known to have colon and breast anti-cancer activities. With an $IC_{50}$ of 44.78 mg/mL, the acetone extract of *A. compactum* demonstrated cytotoxic action against MCF-7 breast cancer cells [68]. Besides isotsaokoin (**14**), Yang et al. [30] also isolated 2 other aldehyde bicyclo nonane compounds from *A. tsao-ko,* namely (1*RS*, 5*SR*, 6*RS*)-5-hydroxy bicyclo [4.3.0] non-2-en-2-carbaldehyde (**18**) and 6-hydroxyindan-4-carbaldehyde (**19**). These were further coupled with (2*E*,6*E*)-8-hydroxy-2,6-dimethyl-2,6-octadienal (**1**), tsaokoarylone (**112**), and (2*E*,8*E*)-10-hydroxy-decadienal (**2**), whose anti-proliferative activities were tested against neuroblastoma N2a murine cells [30]. However, compounds **14**,**18**,**19** had anti-proliferative activity above 200 nM. Furthermore, compounds **1**–**2** and **74** had robust anti-proliferative efficacy, exhibiting $IC_{50}$ values of 46–82 µM.

## Anti-inflammatory

The isolation of Amomaksim A and B from the root of *A. maximum* was initially reported by Yin et al. [40] as these were norlab-terpene compounds with a nine-ring frame. Moreover, compound **30** inhibited lipopolysaccharide-induced macrophages RAW264.7's ability to produce nitric oxide (NO). Yin et al. [37] reported 3 new diarylheptanoids, whose absolute structures were determined with Mosher ester and CD spectra reagents, namely kravanhol A and B (**107**–**108**), as well as renealtin (**109**) from *A. kravanh.* All compounds were reported to have anti-inflammatory activities, with inhibitory effects on NO production in lipopolysaccharide-activated macrophages RAW264.7. The **108** demonstrated this action with an $IC_{50}$ value of 38.9 ± 1.8 mM [50]. It's NO production inhibitory activity strengthent by Zhang et al. [76]. According to Liu et al. [72], the ethanol extract of *A. tsao-ko* suppressed HO-1 and NF-B signals and produced strong anti-inflammatory effects on macrophages stimulated by LPS. Moreover, Zhang et al. [9] isolated **68**, **69**, **70**, quercetin 3-*O*-glucoside (**71**), quercetin-7-*O*-glucoside (**72**), and *meso*-hannokinol (**96**) to confirm active anti-inflammatory activities. The **68** shows remarkable anti-inflammatory characteristics, as seen by its 63.65% inhibition rate on NO generation at 100 mg/mL [9]. From the ethanol extract of *A. tsaoko* fruits, Hong et al. [8] reported the extraction of 2 cycloterpenal (amotsaokonal B and C, (**114**–**115**)) and a new benzaldehyde (amotsaokonal A, **113**). Additionally, each isolate's ability to suppress LPS-induced NO generation in RAW264.7 cells was examined **114** provided the highest anti-inflammatory activity, with an $IC_{50}$ value of 94.8 µM. Two phenylpropanoids (**116**–**117**) that were extracted from the methanol extract of *A. paratsao* fruit were reported by Chai et al. [11]. By preventing the expression of interleukin 6 (IL-6) in activated microglial BV2 cells, they also demonstrated anti-inflammatory properties [11]. The pyranochalcones (**80**–**81**) and pyranoflavanones (**74**–**75**) inhibited the production of NO in lipopolysaccharide-induced RAW 264.7 macrophages, with $IC_{50}$ values ranging from 10.6 to 41.5 µM [46]. They suggested a good anti-inflammatory potential comparable to ibuprofen in the composition of essential oils from *A. subulatum* in Saudi Arabia and India. It showed similar qualitative but different quantitative variations. No significant differences were observed in the pharmacological properties of the essential oils [70]. *A. subulatum* has also immunosuppressive, anti-oxidant and cytotoxic activities [75].

## Anti-fungal

Moon et al. [17] isolated 4 bicyclic nonane aldehydes, namely isotsaokoin and tsaokoin, as well as their $CH_2OH$ side chains (**14**–**16**), as isomers from the methanol extract of *A. tsaoko* fruit. This indicated anti-

fungal activities against trichophyton mentagrophytes, as compound **14** had the highest reaction at 40 μg/mL disk. The **15** was also isolated by Yang et al. [30] with low anti-proliferative activity in the murine neuroblastoma cell line (N2a), with $IC_{50}$ > 200 nM. One of the potential new medical resources for anti-bacterial and anti-fungal medicines is the essential oil of *A. tsao-ko* [17].

### Anti-microbial and Anti-bacterial

GC-MS was used to examine the chemical composition of the essential oil extracted from the dried fruits of *A. tsao-ko*, based on the hydro distillation process. The oil's anti-bacterial efficacy was assessed against 16 different microbes using broth microdilution and agar disc diffusion techniques. Through this procedure, the acyclic monoterpenes mineral, geraniol, and geranial were discovered. The examination of these oil constituents revealed potent anti-bacterial properties against every microbe examined, encompassing both Gram-positive and negative bacteria along with fungi. *Staphylococcus aureus* (CCTCC AB91118) exhibited the greatest bactericidal action, with a minimum inhibitory concentration (MIC) of 0.20 g/L [54]. Additionally, 34 volatile compounds, or 95.4%, were assessed by Cui et al. [71]. The assays for β-carotene/linoleic acid bleaching and DPPH radical scavenging activities yielded $IC_{50}$ values of 5.27 and 0.63 mg/mL for EOs, respectively.

The anti-bacterial activity of fruit extracts from *A. subulatum* and *Elettaria cardamomum* was studied *in vitro* against *Streptococcus mutans*, *Staphylococcus aureus*, *Lactobacillus acidophilus*, *Candida albicans*, and *Saccharomyces cerevisiae*. Acetone, ethanol, and methanol extracts of selected plants showed anti-bacterial activity against all tested microorganisms except *L. acidophilus* [52]. Anti-bacterial activity tests of acetone extract of *A. compactum* were performed using the paper disk diffusion method. This was followed by the determination of the MIC and minimum killing concentration (MBC) against *S. aureus* ATCC 25923. The highest activity was found with an inhibition zone diameter of 8.3 mm and MIC and MBC values of 625.0 μg/mL [68]. The fruit of *A. tsao-ko* also had anti-bacterial activity against *K. pneumoniae* based on the study of Liu et al. [72]. The essential oil of this species has the preservative potential againt *E. coli* [73]. While wreath fruit peel (*A. dealbatum*) *extract* has shown anti-bacterial properties against *S. aureus* and can be used as a natural alternative to conventional antibiotics [62]. Nanocomposite-based anti-microbials, when combined with appropriate antibiotics, can provide synergistic effect and help halt the spread of the global crisis of bacterial resistance [74]. Furthermore, polymer-based nanocomposites facilitate the fabrication of a variety of medical devices due to improved biodegradability and biocompatibility.

### Neuroprotective

Three quercetins were among the flavonoids that Zhang et al. [9] reported being isolated from the ethyl acetate fraction. At 50 mg/mL, **70** exhibited the highest neuroprotective efficacy against $H_2O_2$-induced PC-12 cells while maintaining 78.9% cellular viability. The cytotoxic, immunosuppressive, and anti-oxidant properties of *A. subulatum* extract suggest its use as a neuroprotective agent [74]. Diarylheptanoids from *A. kravanh* can prevent NO formation and may, therefore, be neuroprotective substances [76].

### Platelet Anti-aggregation

Luo et al. [34], isolated 2 new monoterpenes from the ethanol extract of *A. kravanh* fruit, namely (7*S*)-*p*-Simen-2,7,8-triol (**12**) and (3*R*,4*R*,6*S*)-*p*-men-1-en-3,6,10-triol (**13**). The biological activity was reported as an anti-aggregation *in vitro*, namely rabbit platelet-rich platelet (PRP). This was induced by adenosine diphosphate (ADP) at 100 μg/mL, based on the inhibition of **12** and **13** at 34.4% and 30.4%, respectively.

### Anti-diabetic Activity

The ability of natural remedies or medicinal herbs to lessen the gut's or intestine's synthesis and absorption of glucose from digested carbs was assessed. It was stated that they could considerably lower post-prandial hyperglycemia with these techniques. The percentage of α-glucosidase inhibition obtained from the aqueous and methanol extracts of *A. cardamomum* fruit was 10.41% (0.03) and 13.73% (0.02), respectively. Comparably, the percentages of α-amylase inhibition by the methanol and aqueous extracts were 39.93% (0.01) and 82.99%

(0.01), respectively. The *in vitro* anti-diabetic and anti-oxidant properties of the aqueous extracts were demonstrated accurately [58]. Despite prior reports on the anti-obesity qualities of *A. tsao-ko's* crude ethanol extract, Hong et al. [13] managed to isolate the fruit's active ingredients and examine their potential anti-adipogenic effects. Four bioactive compounds were also found from the ethanol extract of *A. tsao-ko* fruits by the bioassay-guided isolation of the phytochemicals: methyl linolenic (**121**), one sesquiterpene alcohol (**122**), and two phenolic compounds (**126**–**127**). When these components' anti-adipogenic properties were assessed in 3T3-L1 cells using oil red O staining, it became clear that treatments with the separated compounds significantly and dose-dependently decreased lipid accumulation D [13]. Plant isolates have anti-diabetic effects due to the presence of various phytometabolites, such as coumarins, alkaloids, and phenols. These compounds contribute to the inhibition of α-glucosidase and α-amylase, which are important in regulating glucose absorption and blood levels. Moreover, novel bioactive compounds derived from plants demonstrate higher anti-diabetic effects than some hypoglycemic drugs used in clinical treatment [77-78].

## ■ CONCLUSION

The other plants in the genus had the potential for exploration as natural products meant that the scientific data available on *Amomum* remained restricted. The *Amomum* species was a focus of much research, both for their potential as novel compounds and their practical biological properties as pure isolates and extracts. Out of the 170 species currently in existence, 53 species which originated in Vietnam, Thailand, China, Korea, and Indonesia were researched. In addition, 9 groups of secondary metabolites, consisting of 127 compounds were obtained, including flavonoids (29.13%), diterpenoids (19.68%), diarylheptanoids 14.96%), monoterpenoids (14.96%), sesquiterpenoid (9.45%) along with other chemical groups (5.51%), steroids (2.36%), phenylpropanoids (1.57%), benzaldehyde and cycloterpenal (2.36%). The biological activities in the *Amomum* genus were revealed including anti-inflammatory, cytotoxic, anti-oxidant, anti-fungal, anti-bacterial, anti-proliferative, anti-cancer, neuroprotective, anti-aggregative platelets, and anti-diabetic properties. Due to the existence of diarylheptanoids and monoterpenoids, the most frequent activity was found to be cytotoxicity against different human cancer cells. Tsaokoarylon (**112**) and hydroxyashabushiketol (**94**) were the most potent for further development as novel natural medicines.

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## ■ CONFLICT OF INTEREST

The authors declare no conflict of interest.

## ■ AUTHOR CONTRIBUTIONS

Deden Indra Dinata collected the literature and wrote the manuscript; Fauzan Zein Muttaqin did data curation; Rani Maharani provided critical inputs in the manuscript preparation. Unang Supratman gave important inputs, oversaw the progress of the study, and assisted with data interpretation and text evaluation. The writers collaborated on the final publication and talked about the findings.

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