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REVIEW ARTICLE

A Review of Onoceranoids from the *Lansium* and *Lycopodium* Genera: Phytochemistry and Their Biological Activities

Rika Septiyanti[1], Rani Maharani[1], Mohamad Azlan Nafiah[2] and Tri Mayanti[1,3*]

[1]*Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Padjadjaran, Jatinangor 45363, Indonesia*
[2]*Department of Chemistry, Faculty of Sciences and Mathematic, Sultan Idris Education University, Tg Malim, Perak 35900, Malaysia*
[3]*PKR Universitas Padjadjaran-BRIN: Drug Discovery from Indonesian Meliaceae Plants, Nanomaterial Microbes, Indonesia*

([*]Corresponding author's e-mail: t.mayanti@unpad.ac.id)

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Abstract

Onoceranoids, a subgroup of triterpenoids, have demonstrated considerable potential in medical applications due to their diverse biological activities. They exhibit antioxidant, cytotoxic, antimutagenic, antibacterial and antifeedant properties. This study aimed to review the phytochemical composition and biological activities of onoceranoids found in the *Lansium* and *Lycopodium* genera. The chemical structures, biological activities, and plant species serving as sources of onoceranoids are analyzed, emphasizing their potential applications in medicine and implications for future research. Experimental approach: Relevant scientific literature on onoceranoids was collected from databases including SciFinder, Google Scholar, and PubMed, covering research from 1967 to 2025. Fifty onoceranoid compounds were identified and analyzed to determine their biological activities and distribution among plant species. The analysis from this review that 96% onoceranoid compounds were found in the *Lansium* genus, establishing these compounds as marker constituents of this genus. Onoceranoids demonstrate extensive biological potential due to their multifunctional bioactivities. These findings support further research on onoceranoid compounds, including their structural modification and potential therapeutic applications in medicine.

Keywords: *Lansium* genus, *Lycopodium* genus, Natural product, Onoceranoid triterpenoid, Pharmacological properties, Phytochemistry, Secondary metabolites

Introduction

Onoceranoids represent a structurally diverse group of natural products, characterized by a common core structure based on the onocerane skeleton [1-3]. This unique framework is composed by cyclohexane rings, marked by an open B ring, giving rise to a plethora of structural variations through modifications such as functionalization and oxidation [4]. Due to their complex chemical structure and functional groups, onoceranoids exhibit a broad range of biological activities [5].

Onoceranoids, as one of the groups of triterpenoids, have been widely studied due to their bioactive properties [6], such as antifeedant [8], antioxidant [9], antidiabetic [10], anticancer [11-12], antibacterial [13] and antimutagenic [14]. Triterpenoids are the largest group of terpenoid-derived secondary metabolites within the scope of natural products [15]. Various types of triterpenoid compounds serve function including defense against herbivores, pathogens, environmental stress, plant communication and interaction with other organisms [16-18].

Triterpenoids are a diverse group of secondary metabolites found in various plant families [19]. Plants that contain many triterpenoids secondary metabolites

include those from Celastraceae [20], Fabaceae [21], Apocynaceae [21], Meliaceae [19, 22], Lycopodiaceae [23], and Schisandraceae family [24]. Onoceranoids are commonly found in the Meliaceae family [25].

Based on reports from journals published between 1967 until 2025, a total of 50 onoceranoid compounds have been identified and classified according to the number of cyclic structures present in each compound, namely bicyclic, tricyclic, tetracyclic onoceranoids, and onoceranoid glycosides. Of these 48 were found in the *Lansium* genus, specifically in the species *L. Domesticum* [26] and *L. parasiticum* [27]. The species *Lycopodium abscurum* was found to contain 2 other onoceranoid compounds [28].

Onoceranoids are an interesting topic to study because they are the most common compounds found in the *Lansium* genus and make them reliable chemical markers for this genus. These compounds are biosynthesized through a complex series of enzymatic reactions, often starting with the cyclization of squalene, a ubiquitous precursor in the biosynthesis of various terpenes [29]. The intricate interplay of enzymes involved in this biosynthetic pathway results in the production of a diverse array of onoceranoid derivatives, each possessing unique structural features and, consequently, distinct biological properties [30]. This paper focuses on onoceranoids obtained from *Lansium* and *Lycopodium* genus, their biological activities, and how these compounds are formed through biogenesis.

Methodology

To ensure a comprehensive review, the study conducted a literature search from PubMed, Scopus, and Google Scholar, focusing on publications from 1967 to 2025. The inclusion criteria involved selecting studies that reported on the structure, biosynthesis, and biological activities of onoceranoid. Specific search terms such as “onoceranoid”, “triterpenoid”, “*Lansium* genus”, and “*Lycopodium* genus” were used to retrieve relevant literature. Additionally, the collected data were analyzed and categorized based on structural characteristics, particularly the number of cyclic rings, as well as biosynthetic pathways and biological activities. These steps were taken to provide a clear and organized overview of the topic.

Plant containing onoceranoids

Onoceranoids from Lansium genus

Several plant families, particularly Lycopodiaceae and Meliaceae, exhibit high concentrations of onoceranoids, reflecting their broad distribution within the plant kingdom. These compounds are often found in the roots, stems, fruit peel, leaves, and flowers of these plants, contributing to their diverse pharmacological activities [31]. Plant extracts rich in onoceranoids have been used for centuries in traditional medicine systems around the world, providing a valuable foundation for modern scientific investigations into their therapeutic potential.

The Meliaceae family, commonly known as the mahogany family, is a diverse group of flowering plants consisting of more than 52 genera with more than 1400 species with one of the genera being *Lansium* [32,33]. This family is widely distributed in tropical and subtropical regions and is recognized for its ecological and economic importance. Members of the Meliaceae family are well-known producers of secondary metabolites, including terpenoids, flavonoids, and alkaloids, which play critical roles in plant defense mechanisms and have been exploited for their pharmacological properties [34].

The *Lansium* genus, particularly the species *Lansium domesticum* and *Lansium parasiticum*, has been extensively utilized in traditional medicine and is a source of bioactive compounds with promising therapeutic potential [35]. *Lansium domesticum* is a fruit-bearing tree widely found in Suriname, Puerto Rico, Australia, and western Southeast Asia, ranging from the Thai Peninsula to Kalimantan, Indonesia [36-38]. *Lansium domesticum* belongs to the Meliaceae family and can grow up to 30 m in height. The taxonomic classification of *Lansium domesticum* Corr. at the variety level by Hasskarl (1844) identified 3 distinct cultivars: duku (*L. domesticum* Corr. var. *duku* Hassk.), kokosan (*L. domesticum* Corr. var. *kokossan* Hassk.), and pisitan (*L. domesticum* Corr. cv. *piedjietan* Hassk.)[39]. Botanically, *Lansium domesticum* is a medium-sized tree characterized by pinnate leaves, small hermaphroditic flowers, and globose to ellipsoid fruits. The fruits are rich in sugars, vitamin C, and essential nutrients, making them a staple in many

tropical regions. The seeds, leaves, and bark are traditionally used for medicinal purposes [40].

Research, shows that terpenoid compounds contained in *Lansium* include: 28% tetranortriterpenoids, 37% onoceranoids, 4% cycloartan, 14% terpenoid glycosides, 7% sesquiterpenoids and 10% steroid [41-45].

Onoceranoids from Lycopodium genus

Lycopodium, commonly known as clubmosses, is a genus of vascular plants within the family Lycopodiaceae [46]. These plants are characterized by their small, needle-like or scale-like leaves and creeping stems. They reproduce via spores produced in specialized structures called strobili [47]. *Lycopodium obscurum*, commonly known as "ground pine" or "princess pine," is a one of species within the *Lycopodium* genus, a group of spore-bearing plants in the Lycopodiaceae family [48]. Native to temperate forests of North America, this species thrives in moist, sandy soils under shaded canopies. Secondary metabolites identified in *L. obscurum* include alkaloids [49] such as lycopodine, clavolonine [50], obscurine, and triterpenoids [51].

Many plants from the *Lycopodium* genus contain α-onocerin, leading to the conclusion that serratane-type triterpenoids originate from the single protonation of α-onocerin. Serratane exhibits pharmacological properties, including cancer chemopreventive effects and inhibition of *Candida albicans* secreted aspartic proteases. In China, Lycopodium obscurum has traditionally been used as a folk medicine for treating contusions, dysmenorrhea, quadriplegia, and arthritic pain, and it has been noted as a source of serratenes

Onoceranoids

Onoceranoids are found in higher plants. According to this literature review, which focuses on studies published between 1967 to 2025, 96% of reported onoceranoids are found in the genus *Lansium* (*L. domesticum* and *L. parasiticum*), in various plant parts including leaves, stem bark, fruit peel, and twigs. Building on these findings, we classify onoceranoids in this review based on the number of their cyclic structures.

Onoceranoid triterpenoids are a type of terpenoid reported to be predominantly found in the *Lansium* genus, characterized by an open-ring structure between C-8 and C-14. In the ^{13}C-NMR spectrum, onoceranoids typically exhibit thirty signals [52], including those corresponding to carbonyl, hydroxyl, sp^3-hybridized carbon, and sp^2-hybridized carbon atoms, with oxygenated carbon atoms commonly observed at C-3, C-21, and C-14 [6]. These compounds exhibit diverse stereochemistry due to the presence of multiple chiral centers, which significantly influences their biological activity. The structure and numbering system of onoceranoid triterpenoids are shown in **Figure 1** [6].

Bicyclic onoceranoids

Bicyclic onoceranoids are a group of onoceranoid-triterpenoids characterized by the presence of 2 cyclic structures in rings B and D or A and B in structure **12**, *seco* structures in rings A, C, and E. The opening of ring C, indicated by the cleavage between C-8 and C-14, is a defining feature of onoceranoids. Additionally, ring E is opened between C-21 and C-22, and ring A is opened between C-3 and C-4. Another hallmark of this structure is the presence of 3 olefinic methylene groups, which is presumed to result from the opening of 3 major rings [53]. Furthermore, this structure is typically characterized by the presence of 2 sp^3-hybridized quaternary carbon atoms.

In 1967, the first onoceranoid, called lansic acid (**1**) was discovered, which has structural characteristics of 2 carboxyl groups, 3 olefinic methyl groups, 2 tertiary methyl groups and 3 terminal methylene groups. As a variant of the onocerin triterpene group, lansic acid features cleavage of both A and E rings, similar to the A ring cleavage in dammarenolic and nyctanthic acids. This distinctive structure, created by a double cleavage, is unprecedented in natural products. Bicyclic onoceranoids are mainly found in the fruit peel of *Lansium domesticum*. However, they have also been identified in the twigs and leaves, as summarized in **Table 1**. The chemical structures of these compounds are presented in **Figure 2**.

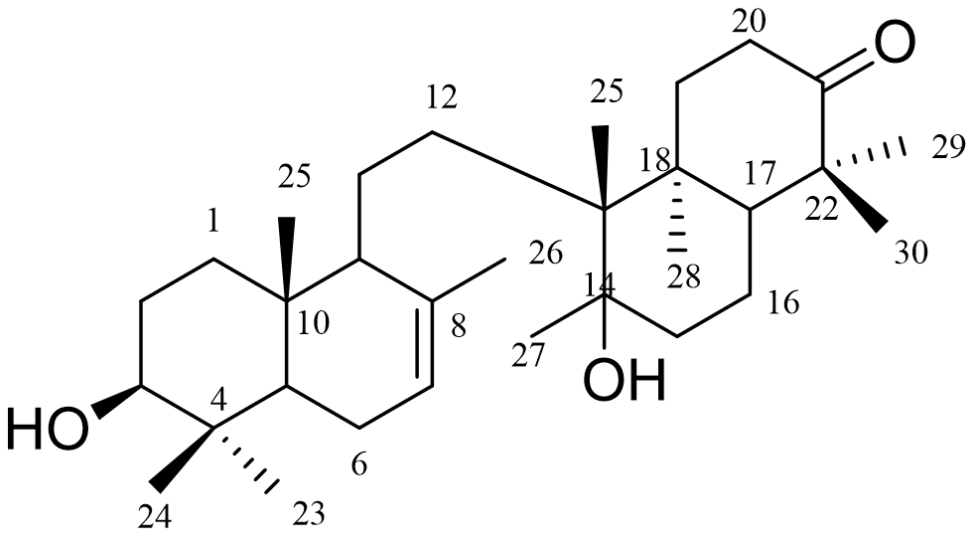

Figure 1 The structure and numbering system of onoceranoid triterpenoids: characterized by an open-ring structure between C-8 and C-14.

Table 1 Plant sources and extraction solvents used for the isolation of bicyclic onoceranoids.

Compound Name	Plant	Plant Parts	Extract	Reference
Lansic Acid (**1**)	*Lansium domesticum* cv. *duku*	Fruit Peel	Light petroleum	[9,54]
Lansic Acid ester (**2**)	*Lansium domesticum* cv. *duku*	Fruit Peel	Ethanol extract	[9]
Lansic acid-3-ethyl ester (**3**)	*Lansium domesticum*	Twigs, Leaves	Ethanol extract	[6,14]
Lansic Acid dimethyl ester (**4**)	*Lansium domesticum* cv. *duku*	Fruit Peel	Light petroleum	[54]
Lansic Acid Diol (**5**)	*Lansium domesticum* cv. *duku*	Fruit Peel	Light petroleum	[54]
Lansic Acid Diacetate (**6**)	*Lansium domesticum* cv. *duku*	Fruit Peel	Light petroleum	[54]
Lansic Acid octahydrodiol (**7**)	*Lansium domesticum* cv. *duku*	Fruit Peel	Light petroleum	[54]
Lansic Acid diacetate (**8**)	*Lansium domesticum* cv. *duku*	Fruit Peel	Light petroleum	[54]
Lamesticumin A (**9**)	*Lansium domesticum*	Twigs, Leaves	Ethanol extract	[6,14]
Enolysis Lamesticumin A (**10**)	*Lansium domesticum*	Twigs, Leaves	Ethanol extract	[6,14]
Lansium Acid V (**11**)	*Lansium domesticum*	Leaves	Methanol extract	[14]
Lamesticumin F (**12**)	*Lansium domesticum*	Twigs, Leaves	Ethanol extract	[14]

Table 2. Plant sources and extraction solvents used for the isolation of tricyclic onoceranoids.

Compound Name	Plant	Plant Parts	Extract	Reference
Lansionic acid (**13**)	*Lansium parasiticum*	Fruit Peel, Leaves	Methanol extract	[14]
Methyl Ester Lansiolate (**14**)	*Lansium domesticum* cv. *duku*	Fruit Peel	Ethanol extract	[9]
Lansium Acid I (**15**)	*Lansium domesticum*	Leaves	Methanol extract	[14]
Lamesticumin E (**16**)	*Lansium domesticum*	Twigs, Leaves	Ethanol extract	[6,14]
Lansium Acid X (**17**)	*Lansium domesticum*	Leaves	Methanol extract	[14]
Lansium Acid II (**18**)	*Lansium domesticum*	Leaves	Methanol extract	[14]
Lansium Acid III (**19**)	*Lansium domesticum*	Leaves	Methanol extract	[14]
Lansium Acid IV (**20**)	*Lansium domesticum*	Leaves	Methanol extract	[14]
Lansiolic Acid (**21**)	*Lansium parasiticum* cv. *duku*	Fruit Peel, Leaves	Methanol extract	[9,14]
Methyl lansiolate (**22**)	*Lansium parasiticum*	Fruit Peel, Leaves	Methanol extract	[14,27]
Ethyl lansiolate (**23**)	*Lansium domesticum*	Twigs, Leaves	Ethanol extract	[6,14]
Lamesticumin B (**24**)	*Lansium domesticum*	Twigs, Leaves	Ethanol extract	[6,14]

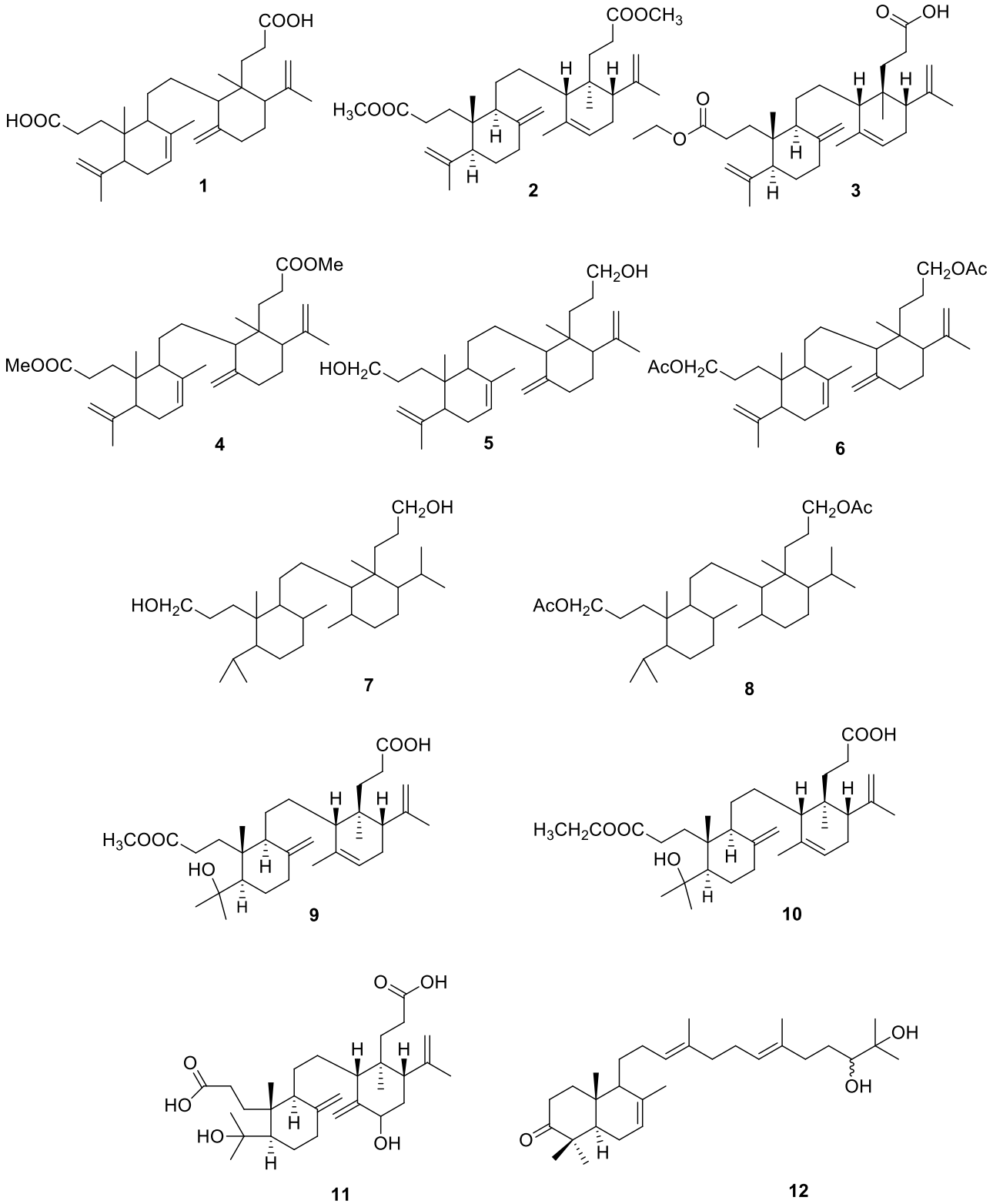

Figure 2 Bicyclic onoceranoids: structure characterized by the presence of 2 cyclic structures in rings B and D (*seco* structures in rings A, C and E) or A and B (*seco* structures in rings C, D and E).

Tricyclic onoceranoids

Tricyclic onoceranoids are a group of onoceranoid-triterpenoids characterized by the presence of 3 cyclic structures in rings A, B and D, *seco* structures in rings C, and E. Tricyclic onoceranoids are mainly found in the leaves of *Lansium domesticum* and *Lansium parasiticum*. However, they have also been identified in the fruit peel and twigs, as shown in **Table 2**. The chemical structures of these compounds are presented in **Figure 3**.

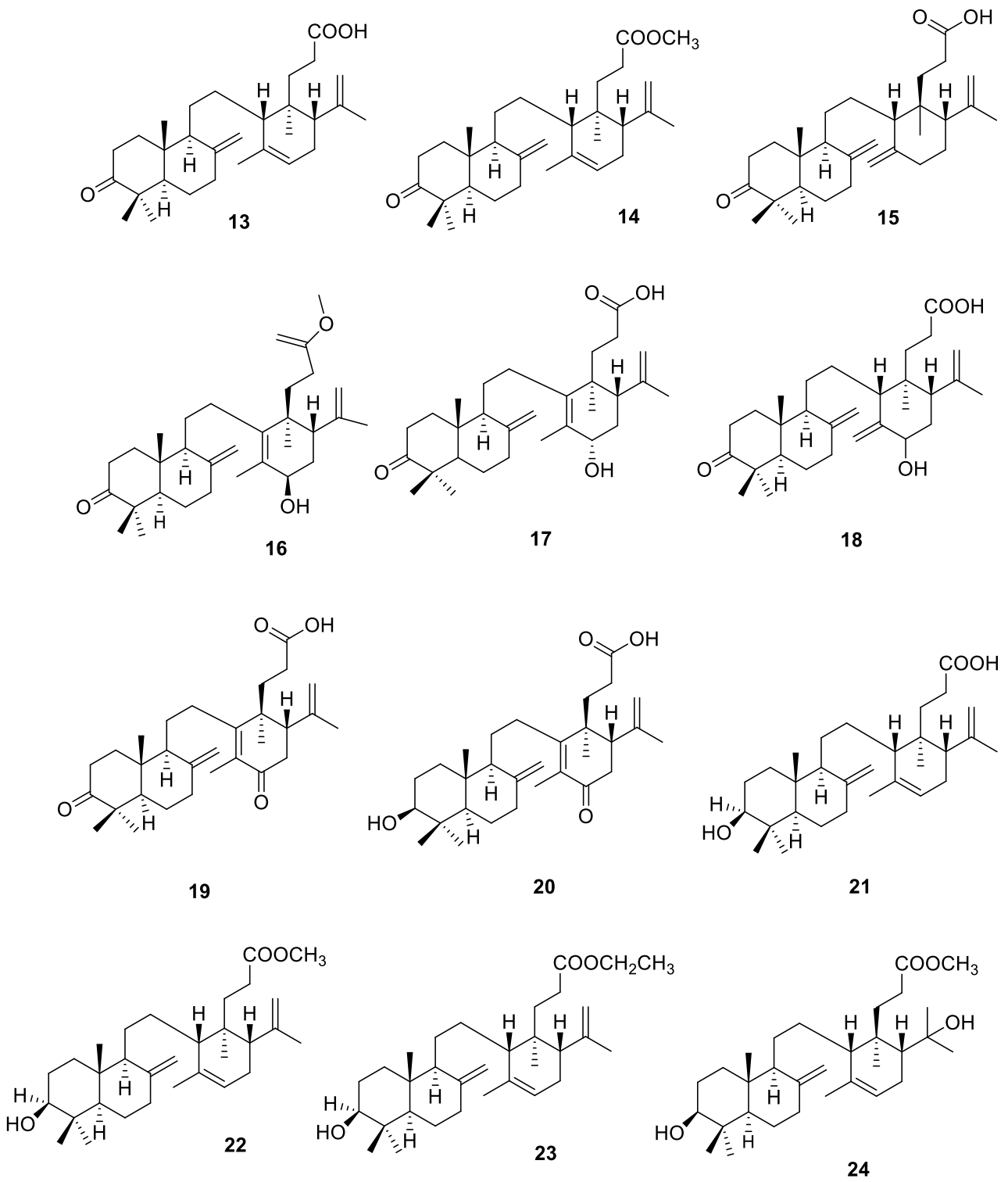

Figure 3 Tricyclic onoceranoids structure: structure characterized by the presence of 3 cyclic structures in rings A, B and D (*seco* structures in rings C and E).

Tetracyclic onoceranoids

Onoceranoids are also found in other genus than *Lansium*, which come from the Lycopodiaceae family (*Lycopodium abscurum*). The structures **36** and **37** is tetracyclic onoceranoid, with a double bond between C-14 and C-15, and oxygenated carbons at C-3 and C-21 [55]. Tetracyclic onoceranoids widely found in nature, are characterized by the presence of 4 cyclic structures in rings A, B, D and E, *seco* structures in rings C. Tetracyclic onoceranoids from plant can be seen in **Table 3**. The structures of these compounds are presented in **Figure 4**.

Glycoside onoceranoids

Glycoside onoceranoids are compound attached to a sugar moiety at the carbon-3 position**.** This unique structural feature results in their frequent occurrence in polar fractions due to the presence of the sugar group**.** Glycoside isolated for the first time by Nishizawa *et al*. [9] namely lansioside which was found from the fruit peel of *Lansium domesticum* cultivar *duku*. From polar fraction, lansioside A (**39**), methyl ester triacetate (**43)**, as well as other onoceranoids compounds **1**, **2**, **22**, and **14** were obtained. Plant sources and extraction solvents used for the isolation of glycoside onoceranoids can be seen in **Table 4**, and the structure can be seen in **Figure 5**.

Biological activity

Although interest in onoceranoids has grown in recent decades, much attention has been directed toward their diverse biological activities. Several studies have demonstrated their antimutagenic, anti-inflammatory, and anticancer properties, which are likely attributed to the configuration of functional groups and the stereochemical orientation of the molecules. According to the literature, of the 50 compounds identified, 77% have been evaluated for their biological activity, whereas the remaining 23% have yet to be investigated, as shown in **Figure 6**.

Table 3 Plant sources and extraction solvents used for the isolation of tetracyclic onoceranoids.

Compound Name	Plant	Plant Parts	Extract	Reference
Lamesticum G (**25**)	*Lansium parasiticum*	Fruit Peel	Ethyl acetate extract	[27]
Lamesticumin D (**26**)	*Lansium domesticum*	Twigs, Leaves	Ethanol extract	[6,14]
α, γ-onoceradienedion (**27**)	*Lansium domesticum*	Fruit Peel	Hexane extract	[56]
α-onoceradienedione (**28**)				[54]
8,14-secogammacera-7,14-diene-3,21-dione (**29**)	*Lansium domesticum* cv. *kokossan*	Leaves	Methanol extract	[14,57]
8,14-secogammacera-7,14(27)-diene-3,21-dione (**30**)	*Lansium domesticum*	Bark	Methanol extract	[57]
Kokosanolide B (**31**)	*Lansium domesticum* cv. *kokossan*	Seed	Methanol extract	[58]
21α-hydroxyonocera-8(26),14-dien-3-one (**32**)	*Lansium domesticum*	Peel	Methanol extract	[53]
3β-hydroxyonocera-8(26), 14-diene-21-one (**33**)	*Lansium parasiticum*	Fruit Peel	Ethyl acetate extract	[27]
3-Hydroxy-8,14-secogammacera-7,14-dien-21-one (**34**)	*Lansium domesticum* cv. *kokossan*	Fruit Peel	Hexane extract	[59]
Lamesticumin C (**35**)	*Lansium domesticum*	Twigs, Leaves	Ethanol extract	[6,14]
(3α,8 β,14 α,21β)-26,27-dinoronocerane-3,8,14,21-tetrol (**36**)	*Lycopodium abscurum*	Whole Plant	Methanol extract	[28]
26-nor-8 β -hydroxy- α -onocerin (**37**)	*Lycopodium abscurum*	Whole Plant	Methanol extract	[28]
Iso-onoceratriene (**38**)	*Lansium domesticum* cv. *duku*	Fruit Peel	Petroleum extract	[54]

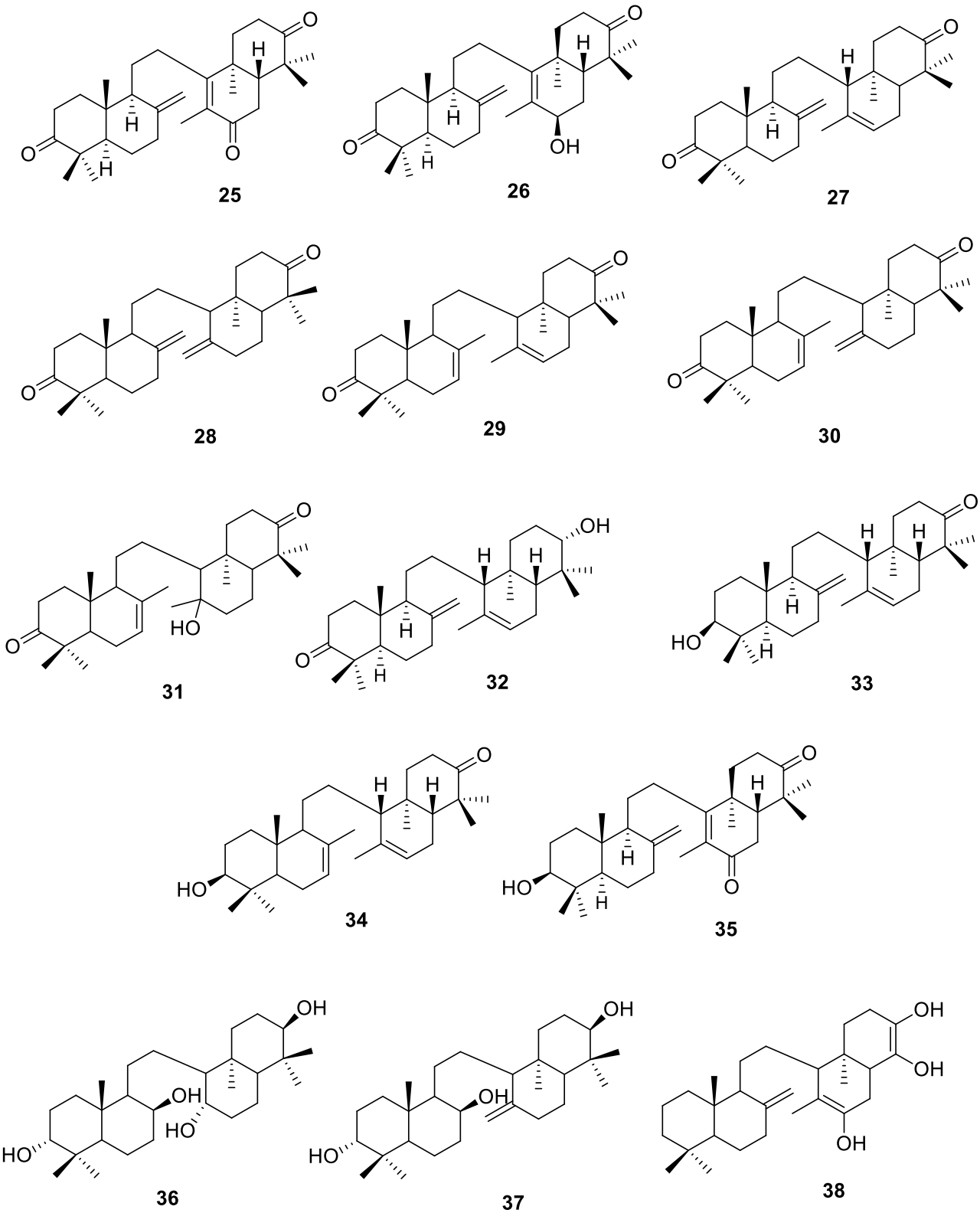

Figure 4 Tetracyclic onoceranoids: structure characterized by the presence of 4 cyclic structures in rings A, B, D and E (*seco* structures in rings C).

Table 4 Plant sources and extraction solvents used for the isolation of glycoside onoceranoids.

Compound Name	Plant	Plant Parts	Extract	Reference
Lansioside A (**39**)	*Lansium domesticum* cv. *duku*	Fruit Peel	Ethanol extract	[9]
Lansioside B (**40**)	*Lansium parasiticum*	Fruit Peel, Leaves	Polar fraction	[10,14]
Lansioside C (**41**)	*Lansium parasiticum*	Fruit Peel, Leaves	Polar fraction	[10,14]
Methyl lansioside C (**42**)	*Lansium parasiticum*	Fruit Peel	Polar fraction	[10]
Methyl ester triacetate (**43**)	*Lansium domesticum* cv. *duku*	Fruit Peel	Ethanol extract	[9]
Lansium Acid VI (**44**)	*Lansium domesticum*	Leaves	Methanol extract	[14]
Lansium Acid VII (**45**)	*Lansium domesticum*	Leaves	Methanol extract	[14]
Lansium Acid VIII (**46**)	*Lansium domesticum*	Leaves	Methanol extract	[14]
Lansium Acid IX (**47**)	*Lansium domesticum*	Leaves	Methanol extract	[14]
Lansium Acid XI (**48**)	*Lansium domesticum*	Leaves	Methanol extract	[14]
Lansium Acid XII (**49**)	*Lansium domesticum*	Leaves	Methanol extract	[14]
Lansioside E (**50**)	*Lansium domesticum* cv. *kokossan*	Fruit Peel	Hexane extract	[60]

Antifeedant

Antifeedants are substances (natural or synthetic compounds) that deter or prevent pests especially insects from feeding [61]. They play a crucial role in pest management by deterring herbivores from consuming plant material, thus protecting crops from damage. Many antifeedants are unpalatable or toxic to insects, leading them to avoid the treated plants [62]. For example, certain triterpenes have been shown to completely prevent feeding in larvae within a short time frame, leading to starvation if they remain on the plant [63]. Some antifeedants may distort the normal function of neurons that perceive feeding stimuli, effectively reducing the insect's desire to feed [64]. This can occur through the stimulation of specialized receptors that detect deterrent compounds [65,66]. Onoceranoids from seed and bark *Lansium domesticum* cultivar *Kokossan* have antifeedant activity against *Epilachna vigintioctipunctata* larvae and the methanol extract of this plant also has a potent antifeedant activity as shown in **Table 5** [8].

Table 5 summarizes the reported antifeedant activity of onoceranoids **29**-**31**, which were tested at a concentration of 1% in antifeedant assays using *Solanum nigrum* leaves against fourth instars larvae of *Epilachna vigintioctopunctata* [8]. Among these, compound **31** has been noted to exhibit the highest activity with 99%, followed by compound **29** with 85%, and compound **30** with 56%. The presence of a hydroxyl (-OH) group in compound **31** is suggested to contribute to its enhanced antifeedant effect, possibly by facilitating stronger interactions with larval target receptors. These observations indicate that onoceranoids isolated from *Lansium domesticum* cultivar *kokossan* may serve as promising natural antifeedant agents. The reported activities align with previous findings on the efficacy of plant-derived compounds in insect pest control [8].

Besides that, onoceranoid compounds isolated from *Lansium domesticum* exhibited significant antifeedant activity against the rice weevil (*Sitophilus oryzae*) [7], a major pest of stored grain products. These compounds significantly reduced feeding consumption at concentrations of approximately 0.5% weight/weight (w/w). The antifeedant activity was evaluated using a flour disk bioassay, in which hard red spring wheat flour disks were uniformly treated with aqueous solutions of the test compounds at varying concentrations and subsequently exposed to *S. oryzae*. Negative controls consisted of flour disks treated with water only, establishing baseline consumption levels standardized to 100%. Multiple range test using Tukey's test ($p < 0.05$), the same letters denote treatments not significantly different from each other. The antifeedant activity against *Sitophilus oryzae* can be seen in **Table 6** [7].

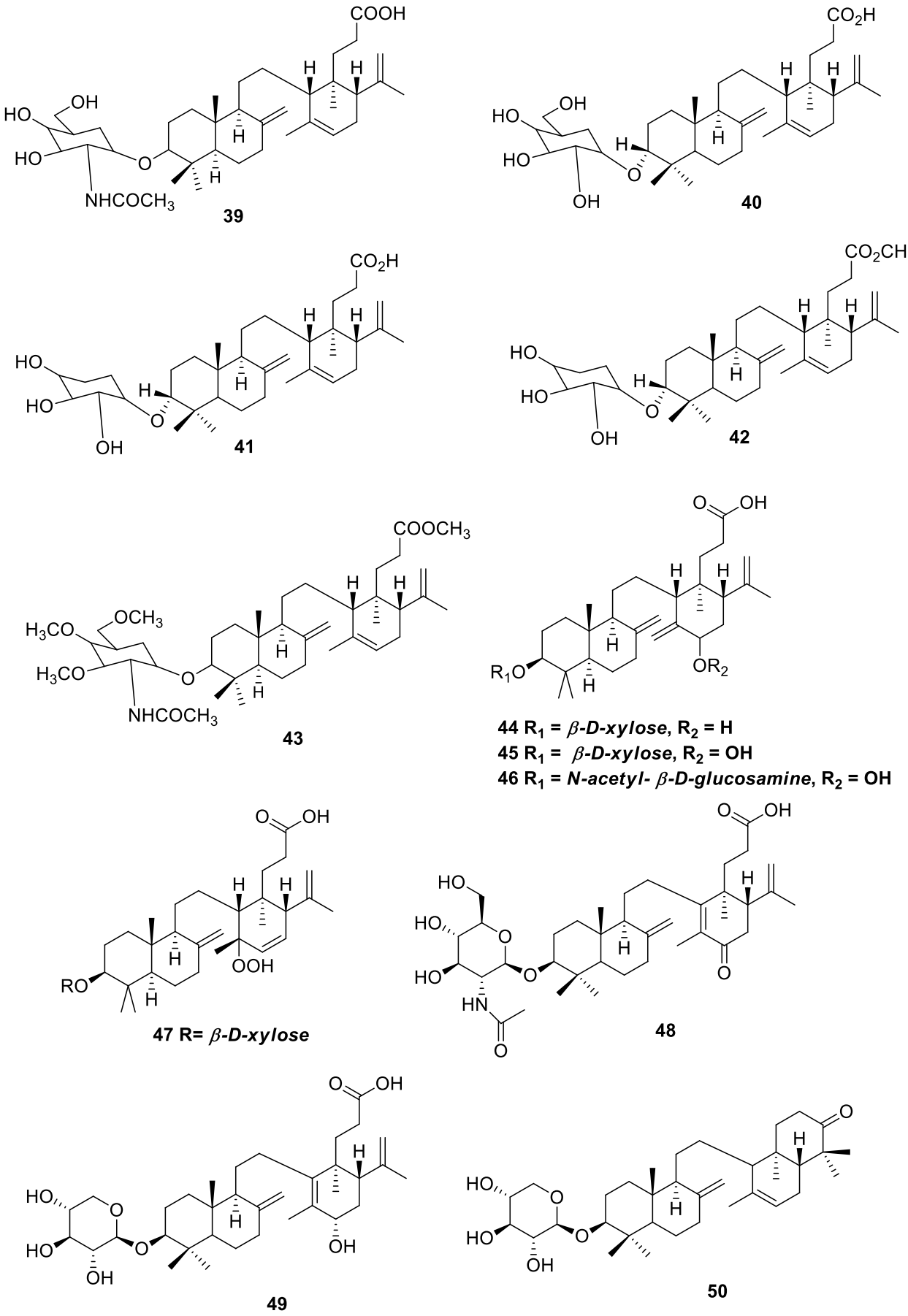

Figure 5 Glycosides onoceranoid structure**:** onoceranoids that are attached to a sugar moiety at the carbon-3 position.

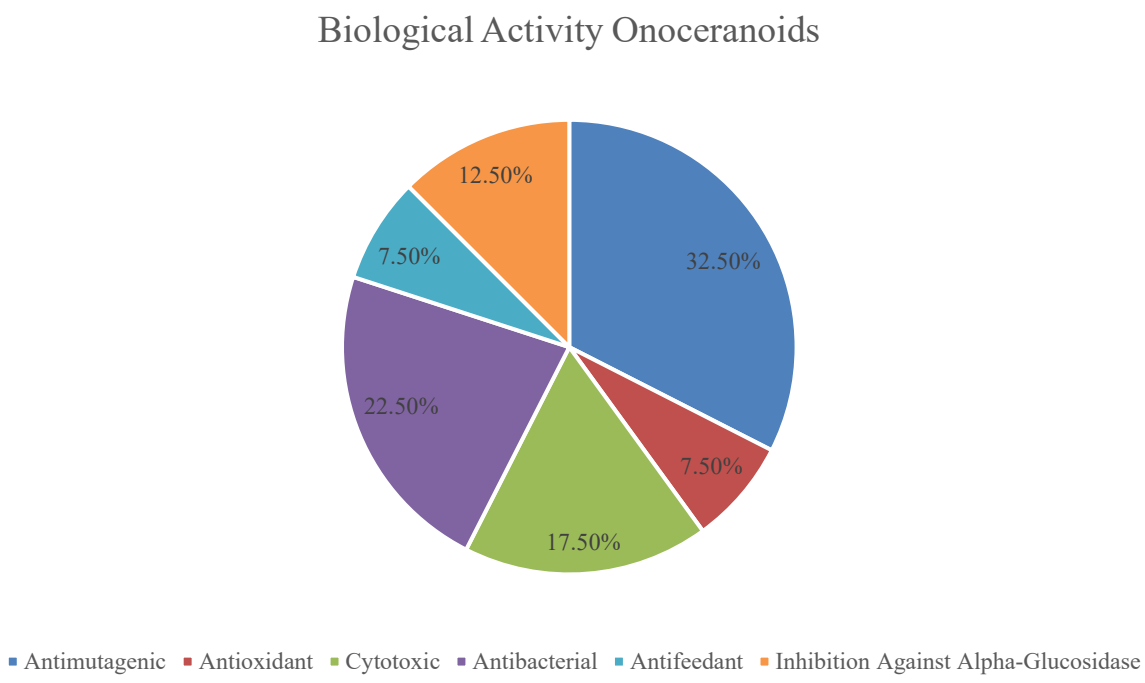

Figure 6 Biological activity of onoceranoids.

Table 5 Antifeedant activity of onoceranoids compound **29-31** against *Epilachna vigintioctipunctata* larvae.

Compound (conc. 1%)	Antifeedant activity%
29	85
30	56
31	99

Table 6 Antifeedant activity of onoceranoids compound against *Sitophilus oryzae.*

Compound (conc. 0.5% w/w)	Consumption of diet (% control ± SEM)	*p*-value
*Negative control	100.0 ±10.2a	
18	56.1 ± 4.5b	< 0.01
21	63.2 ± 3.8b	< 0.01
27	40.1 ± 6.2b	< 0.001
38	64.7 ± 7.5b	< 0.05

*flour disks treated with water only

Table 7 Free radical scavanging activities effect.

Compound	Scavenging Capacity /SC_{50} (mM)
40	13.7
41	23.6
42	14.5
Ascorbic acid	2.45

Table 6 summarizes the reported antifeedant activity of onoceranoids against *Sitophilus oryzae.* Compared to the controls, disks treated with onoceranoid compounds showed a significant decrease in consumption, demonstrating potent feeding deterrent effects. Structural variations among the onoceranoid compounds influenced their efficacy. For instance, the presence of two keto groups in onoceradienedione (**27**) enhanced antifeedant activity relative to iso-onoceratriene (**38**), suggesting that specific keto substitutions may improve interactions with insect chemoreceptors. In contrast, the addition of a keto group at the 3-position in lansiolic acid (**21**) reduced antifeedant activity, highlighting the importance of substituent position in modulating biological effects. These findings contribute to a better understanding of the structure-activity relationships of onoceranoids and their potential application as natural antifeedant [7].

Antioxidant

Antioxidants are important for defending biological systems from oxidative stress, resulting from an imbalance between reactive oxygen species (ROS) and the body's detoxification mechanisms [67]. The mechanisms of antioxidant action include direct scavenging of free radicals, metal ion chelation, and modulation of antioxidant enzyme activity. Specifically, antioxidants can counteract free radicals by either transferring a hydrogen atom (HAT) or facilitating a single electron transfer (SET), thereby effectively preventing oxidative reactions that can damage cells [68]. Additionally, they can inhibit the activity of enzymes that generate free radicals or increase the levels of endogenous antioxidant enzymes like catalase (CAT) and superoxide dismutase (SOD) [69-71].

Onoceranoids exhibit promising antioxidant properties that align with these mechanisms. Their chemical structure allows them to scavenge ROS effectively and chelate transition metals, thereby reducing oxidative damage. Studies suggest that onoceranoids can modulate redox signalling pathways, enhancing the body’s intrinsic defences against oxidative stress [72]. This dual action direct scavenging and indirect modulation positions onoceranoids as potentially beneficial compounds in therapeutic contexts aimed at mitigating oxidative stress-related diseases. Onoceranoids belonging to the triterpene xyloside type from fruit peel *Lansium parasiticum* have been isolated from the polar fraction. Interestingly, triterpene glycosides contain a rarely found sugar, N-acetylglucosamide. Compounds **42** and **40** demonstrated moderate radical scavenging activity, while compounds **41** exhibited weak radical scavenging activity as shown in **Table 7** [10].

Compounds 40 and 42 have been reported to exhibit moderate antioxidant activity by effectively scavenging free radicals, as demonstrated in the DPPH assay with ascorbic acid as a reference compound [10]. Structurally, compound 40 prossesses additional hydroxyl groups, which may contribute to its slightly higher activity compared to compound 42. Conversely, the relatively lower free radical scavanging activities effect in compound 41 has been attributed to structural differences, including the absence of methyl esters and fewer hydroxyl groups, potentially reducing its capacity to donate electrons and neutralize free radicals. These observations highliht the potential of onoceranoids as natural antioxidants for mitigating oxidative stress-related conditions. These findings are consistent with previous studies that have shown plant-derived triterpenes in scavenging free radicals [73]. Further investigations into the structure-activity relationships of these compounds are suggested to better understand the molecular mechanisms behind their antioxidant effects.

Inhibition against alpha-glucosidase

Inhibition of α-glucosidase is a key mechanism by which certain compounds can help manage hyperglycemia and type 2 diabetes [74]. α-glucosidase is an enzyme that is responsible for the conversion of carbohydrates into glucose, which is absorbed into the bloodstream. Inhibiting this enzyme slows glucose absorption, leading to decreased blood glucose levels after meals [75].

Onoceranoids have shown promising α-glucosidase inhibitory activity [76]. The α-glucosidase inhibition assays mentioned in these studies were performed *in vitro*, involving the enzymatic breakdown of sucrase and maltase to produce glucose residues [77]. Compounds **40**, **41** and **42** were also tested for inhibitory against α-glucosidase, but did not show to inhibit α-glucosidase [78].

Postprandial hyperglycemia (PH) is an early indicator of type 2 diabetes (T2D) and serves as a significant target for antidiabetic therapies [79]. Managing PH can be accomplished by inhibiting the enzyme α-glucosidase in the intestines, which plays a critical role in the breakdown of oligosaccharides [80]. This inhibition results in a reduction of glucose released from oligosaccharides and slows down glucose absorption into the bloodstream, thus assisting in the management of T2D [81]. Fruit peel extract from *Lansium parasiticum* has potential promising inhibition (IC_{50} 2.5 – 4.3 mg/mL) and there is a compound isolated from that extract, which is lamesticumin G, showeing weak inhibition against α-glucosidase with an IC_{50} of 2.27 mM [27].

Cytotoxic activity

Cytotoxic activity is a complex process that encompasses several mechanisms, such as the triggering of apoptosis, the generation of oxidative stress, cell cycle arrest, and damage to DNA [82]. Cytotoxic activity refers to the ability of certain compounds to induce the death of cells, particularly in cancer cells. This activity is a crucial aspect of cancer therapy, aiming to eliminate malignant cells while sparing normal cells. Natural products are known for their cytotoxic effects, with onoceranoids being one of them [83-86].

There are onoceranoids from the methanol extract of fruit peel of *L. domesticum* including compounds **13**, **33**, **32** and **1**. The methanol extract was tested on brine shrimp (*Artemia salina*) at 100 µg/mL and had a moderate cytotoxic activity [53]. Besides that, hexane extract from fruit peel of *L. domesticum* Corr. contains onoceranoid; compound **34** and **50** and has cytotoxic activity against MCF-7 with IC_{50} value of 717.5 µM and 39.83 µg/mL respectively [59,60].

Compound **30** which is included in the onoserandiendion isolated from fruit methanolic extract of *Lansium domesticum* Corr. (Langsat) and tested against HeLa (cervical), T47D (breast) and A549 (lung) cell lines using MTT and XTT assay. Compound **30** demonstrated weak activity against A549 (IC_{50} 13.71 µg/mL), HeLa (32.39 µg/mL) and T47D (30.69 µg/mL) cell lines [87]. Compound **29** from *Lansium domesticum* demonstrated notable inhibition activity against MCF-7 cells, with an IC_{50} of 29.73 µg/mL while tamoxifen exhibited an IC_{50} of 20.5 µg/mL [57].

In silico tests were also carried out on several types of onoceranoid compounds using molecular docking, Lipinski's rule of 5, *in silico* ADMET (Absorption, Distribution, Metabolism, Excretion, dan Toxicity), and molecular dynamics simulations [88]. Compound **29** has a potential inhibitor of Erα. This observation suggests a hypothesis that these compounds could function as antagonist ligands, similar to 4OHT (4-hydroxytamoxifen). Collectively, these findings provide valuable insights into the potential therapeutic significance of these triterpenes in targeting ERα-associated breast cancer [89].

Antibacterial activity

Antibacterial agents, commonly referred to as antibiotics, have transformed modern medicine by offering effective treatments for bacterial infections. The discovery and advancement of antibiotics have saved innumerable lives and remain an essential part of global healthcare [90,91]. However, the overuse and misuse of antibiotics have led to the alarming rise of antibiotic-resistant bacteria, posing a significant threat to public health [91]. In recent years, there has been a growing interest in exploring alternative antibacterial agents from natural sources, such as medicinal plants and marine organisms [92]. Nine compounds isolated by Dong *et al.* [6] from the twigs of *Lansium domesticum* Corr. have activity against Gram-positive bacteria **Table 8**.

Minimum inhibitory concentration (MIC) values have been reported as the lowest concentrations required to inhibit visible bacterial growth. Each test was performed in triplicate, and compounds with MIC values exceeding 50 µg/mL were considered inactive, with magnolol serving as the positive control. Structural characterization of the compounds was conducted using comprehensive spectroscopic analysis, and the absolute configuration of C-21 in compound 12 was determined by Snatzke's method. Compound 12 has demonstrated potent antibacterial effects, with MIC values ranging from 6.25 to 12.5 µg/mL against various bacterial strains [93,94]. The presence of a conjugated ketone group in the A-ring and a hydroxyl (-OH) group at C-21 has been suggested to play a critical role in its biological activity. The hydroxyl group at C-21 may enhance interactions with bacterial cell membranes or enzymes, potentially disrupting key processes essential for bacterial survival.

Furthermore, the extended aliphatic chain with double bonds is thought to increase hydrophobicity, facilitating interactions with lipid membranes of Gram-positive bacteria [93,94].

Table 8 Antibacterial activity onoceranoids compound.

Bacteria	MIC (*μ*g/mL)									
	A	**3**	**9**	**10**	**12**	**16**	**23**	**24**	**26**	**35**
S. aureus	25	50	6.25	> 50	> 50	> 50	6.25	6.25	> 50	6.25
S. epidermis	12.5	12.5	12.5	12.5	> 50	> 50	12.5	12.5	> 50	12.5
M. luteus	12.5	> 50	6.25	> 50	> 50	> 50	6.25	3.12	> 50	6.25
B. subtilis	12.5	12.5	3.12	12.5	12.5	12.5	3.12	3.12	6.25	3.12
M. pyogenes	25	12.5	3.12	50	> 50	6.25	3.12	3.12	> 50	3.12
B. cereus	12.5	3.12	3.12	3.12	3.12	3.12	3.12	3.12	3.12	3.12

*A: representing magnolol, was applied as a positive control.

Antimutagenic activity

Antimutagenic compounds play a crucial role in cancer prevention by inhibiting the mutagenic effects of various environmental agents [95]. Among these compounds, onoceranoids, a class of triterpenoids derived from several plant species, have garnered attention for their potential health benefits. These compounds are characterized by their unique structural features, which contribute to their biological activities, including antimutagenic properties [96]. Recent studies have demonstrated that certain onoceranoids triterpenes exhibited significant antimutagenic effects against well-known mutagens such as Trp-P-1 and PhIP, which are heterocyclic amines commonly found in cooked meats [97]. For instance, lansiolic acid (**21**) and lansionic acid (**13**) have shown remarkable inhibition rates of 73.8% and 79.9%, respectively, against Trp-P-1 at specific concentrations, comparable to established antimutagenic agents like nobiletin [89,98]. Onoceranoids from leaves of *Lansium domesticum* showed antimutagenic effect against 3-amino-1,4-dimethyl-5H-pyrido[4,3-b]indole (Trp-P-1) and 2-amino-1-methyl-6-phenylimidazo [4,5-bI]pyridine (PhIP) using the Ames assay. Moreover, oral intake of a major constituent, lansionic acid (**13**), showed antimutagenic effects against PhIP in an *in vivo* micronucleus test. The mechanisms underlying the antimutagenic effects of onoceranoids may involve the modulation of metabolic pathways that activate or detoxify mutagens, thus preventing DNA damage. Furthermore, structure-activity relationship studies indicate that the presence of specific functional groups, such as carboxylic acid moieties, enhances the antimutagenic efficacy of these compounds [99].

Onoceranoids biogenesis

Onoceranoids are secondary metabolites that are often found in the genus *Lansium* and *Lycopodium,* which are included in the triterpenoid group. Triterpenoids are composed of 6 isoprene units to produce squalene [100,101]. Based on the biosynthetic pathway, triterpenoids are formed from 2 main pathways, namely the mevalonic acid (MVA) pathway which occurs in the cytosol with the initial precursor acetyl-CoA and the methylerythritol phosphate (MEP) pathway which occurs in the plastid with the precursors pyruvate and glyceraldehyde-3-phosphate/G3P [102] as shown in **Figure 8**.

Onoceranoid triterpenoids have a unique characteristic ring structure that opens at C-8 and C-14 by oxidosqualene cyclase enzyme. The onoceranoids derivatives can be synthesized through a skeleton that alters the position of the double bond untilizing 1,3-hydride shift, oxygenation, dehydrogenation, and hydroxylation. The biosynthesis of each compound is fascinating because many of them differ only slightly, such as in the functional groups at C-3 and C-21 or the position of the double bond at C-7/C-8, C-8/C -26, C-14/C-15, and C-14/C-27 [19]. The biogenesis of onoceranoids has been proposed to involve tetrahymanol, an onoceranoid precursor, through rearrangement of the A and E rings via photolysis. UV

light irradiation induces the photolysis of 3-oxo-type triterpenoids, leading to the formation of 3,4-seco free acids, which causes the opening of the A and E rings in onoceranoids. Another ring-opening reaction can occur via Baeyer–Villiger oxidation [100,103,104]. The formation of onoceranoids from squalene is thought to use the enzyme tetrahymanol cyclase to form tetrahymanol, which is an onoceranoid precursor as shown in **Figure 9**.

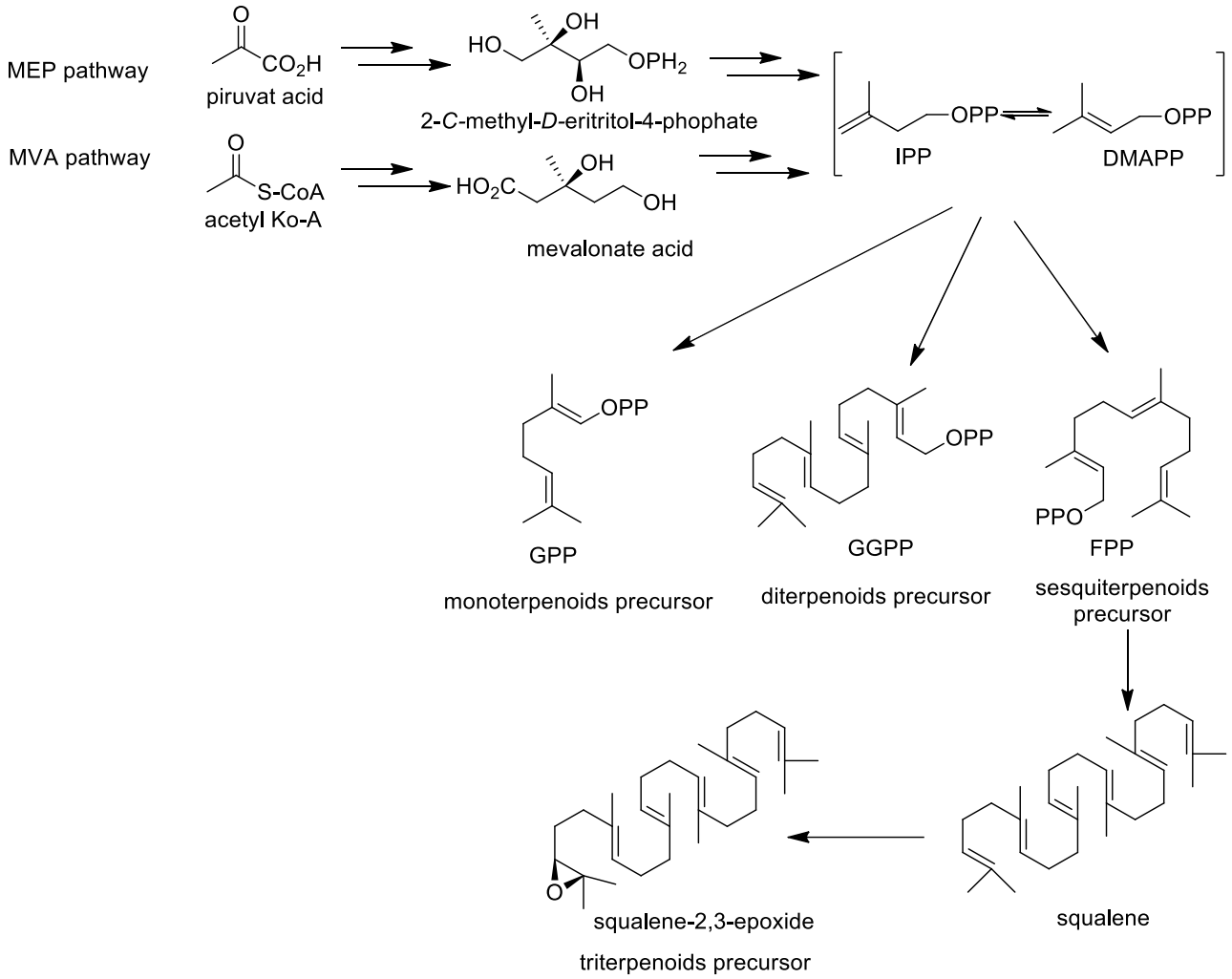

Figure 8 Triterpenoid biosynthesis.

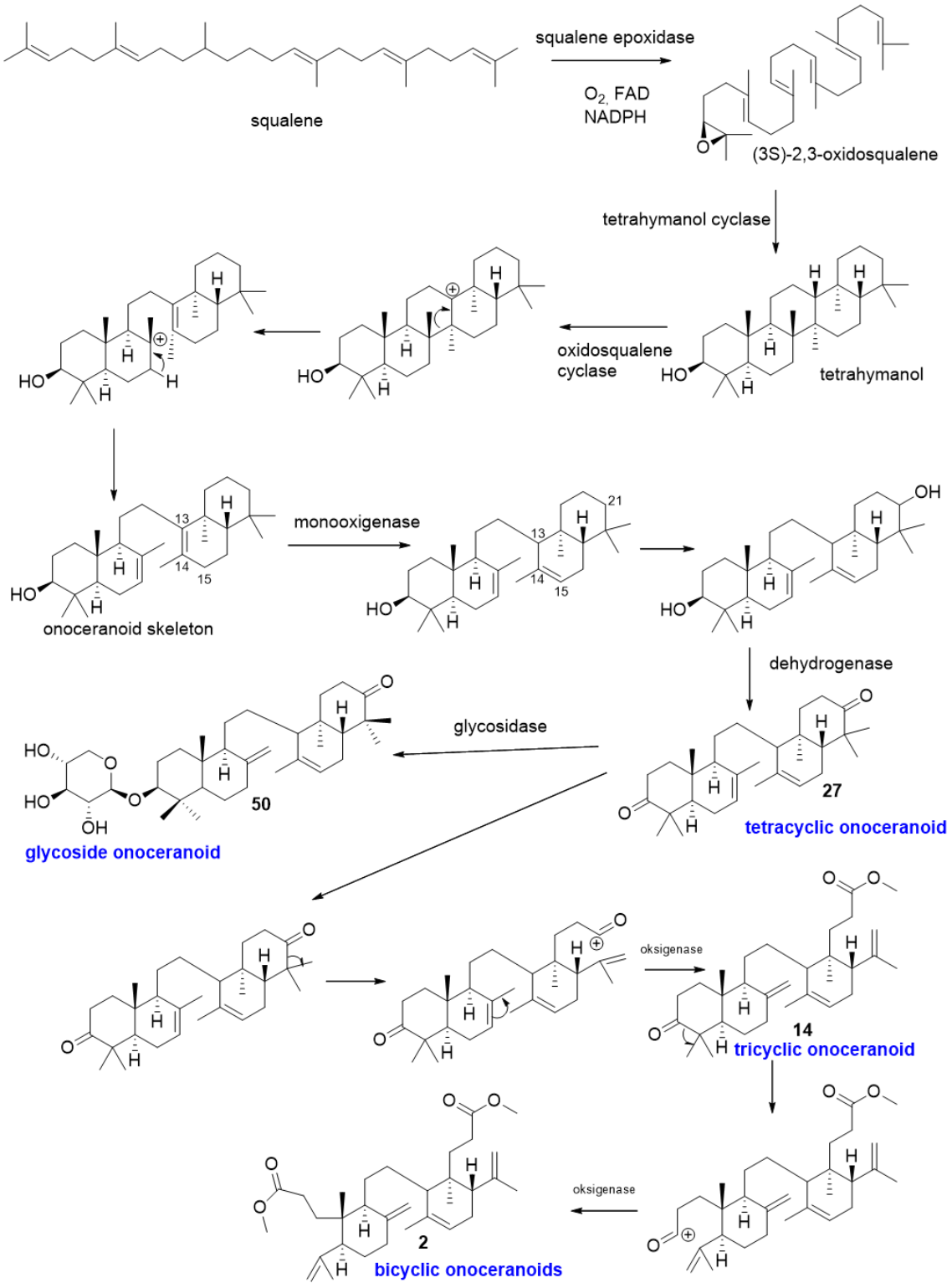

Figure 9 Biogenesis onoceranoids from (3S)-2,3-oxidosqualene: The pathway involves a series of enzymatic transformations catalyzed by specific enzymes, including squalene epoxidase, tetrahydromanol cyclase, oxidosqualene cyclase, monooxygenase, dehydrogenase, and glycosidase. These enzymes facilitate the conversion of squalene through intermediate structures such as (3S)-2,3-oxidosqualene and tetrahydromanol, ultimately leading to the formation of various onoceranoid derivatives. This pathway represents the proposed mechanism by which onoceranoid compounds are biosynthesized in nature.

Conclusions and future perspectives

We give a summary of onoceranoids, a group of triterpenoids, highlighting their diverse and promising biological activities. Highly oxygenated onoceranoid glycosides, such as compounds **40** and **42** exhibited potent antioxidant effects. Regarding cytotoxicity, bicyclic compounds **1** and **13**, tetracyclic compounds **30** – **34**, and glycoside onoceranoid (**50)** isolated from *Lansium domesticum* showed moderate to weak activity against various cancer cell lines, with compound **29** notably inhibiting MCF-7 breast cancer cells and displaying potential as an ERα inhibitor *in silico*. The bicyclic onoceranoid compound **12**, featuring 2 hydroxyl groups, demonstrated strong antibacterial activity with low MIC values. Additionally, the tetracyclic compound **31**, with 2 ketone groups and 1 hydroxyl group, showed the highest antifeedant activity, achieving 99% inhibition against *Epilachna vigintioctopunctata* larvae. While some compounds, like lamesticumin G, exhibited weak α-glucosidase inhibition, no onoceranoids with strong activity against this enzyme have been reported. This information can be used as reference for isolating onoceranoids from plants or as a reference for exploring their biological activity in various fields. These findings suggest that onoceranoids, abundant in the *Lansium* genus and present in *Lycopodium*, hold significant potential for medical and agricultural applications. Further toxicity and *in vivo* studies are needed to confirm their efficacy and safety. Future work should focus on elucidating molecular mechanisms, optimizing synthetic, and clinical validation, alongside biotechnological and industrial development for anticancer, pest control, and antibiotic alternative applications.

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CRediT Author Statement

T Mayanti: Conceptualization, methodology, review, supervision, and funding acquisition. **R Septiyanti:** Resources, investigation, writing original draft, data curation, editing and visualization. **R Maharani:** review, supervision and editing. **M A Nafiah:** review and supervision.

Declaration of Generative AI in Scientific Writing

During the writing of this manuscript, the authors used generative AI technologies to assist with language refinement, grammar correction, and the improvement of scientific clarity. The AI tools were employed solely for linguistic; all intellectual content, data interpretation, analysis, and conclusions were developed and critically reviewed independently by the authors. The authors take full responsibility for the integrity and originality of the content presented in this article.

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