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A review on the Phytochemistry and Pharmacological Activities of some Species from Genus *Dodonaea* (Sapindaceae Family)

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ABSTRACT

This review focuses mainly on findings of the chemistry and pharmacological activities of some plant species from genus *Dodonaea*. The continued chemical studies of *Dodonaea* species such as *D. viscosa*, *D. angustifolia*, *D. spatulata*, *D. polyandra* and *D. ceratocarpa* and the related plants have resulted in isolation of flavonoids, terpenoids, coumarins and their glycosides, among other classes of compounds. The presence of these compounds is thought to be responsible for the various pharmacological activities the plant species possess. Extracts and isolated compounds from various species of *Dodonaea* plants have been reported to exhibit a range of activities including but not limited to antioxidant, anti-inflammatory, antimicrobial, antiplasmodial, anticancer, antidiabetic and antiviral activities.

Keywords: *Dodonaea*, Flavonoid, Terpenoid, Antimicrobial, Anti-inflammatory, Antioxidant.

INTRODUCTION

Medicinal plants have received great attention in the recent past as an alternative form of therapy and medication that supports local health care systems of both developed and developing communities [1]. Published World Health Organization (WHO) reports reveal that about 80% of the world's population uses medicinal plants to manage and cure diseases [2]. Their application in therapy and medication has increasingly gained public acceptance and interest from scientific community owing to their good therapeutic performance and minimum adverse effects on humans and the environment [1,3]. These plants are processed and taken in different forms, including as whole herbs, concoctions, plant concentrates, essential oils, and formulations into tablets and capsules that contain a powdered form of a raw herb or crude extract [4]. Many plant-derived compounds have also been used as drugs, either in their original or semi-synthetic form, in addition to serving as drug precursors, drug prototypes and pharmacological probes [3].

Dodonaea species are among medicinal plants whose leaves, stems and fruits are widely used in traditional medicine formulations [1]. *Dodonaea* is a genus in the *Sapindaceae* family comprised of more than 70 recorded species [1]. The species are majorly flowering plants whose ethnobotanical reports attach great value on leaves, stems and fruits. The plants are widely distributed in tropical and temperate region of Africa, America, Asia and Australia [1]. The most extensively studied species of *Dodonaea* genus are, *D. viscosa* and *D. angustifolia*. Both of them are medium-sized shrubs widely distributed in in Australia, Africa, Asia and South America. *D. viscosa* originated from Australia but it also occurs throughout the tropics, subtropics and temperate regions of Africa, North America, South America and Asia [1, 5-8]. Other fairly studied species are *D. spatulata*, *D. polyandra* and *D. ceratocarpa*.

Most of these plants from *Dodonaea* genus have been traditionally used in the treatment of scurvy, inflammation, kidney pain, sore throat, intestinal parasite, herpes, wounds burn, rheumatism, cough, backache, toothache, skin burn, skin infection, tumor and wound healing [1,5,6]. Scientific investigations have reported a good number of pharmacological activities associated with *Dodonaea* plant species. The pharmacological activities of these plants have been attributed to the presence of bioactive compounds. This paper reviews the studies on *Dodonaea* species with respect to their isolated chemical compounds and their pharmacological activities.

Phytochemicals Isolated from *Dodonaea* Species

Flavonoids

Flavonoids are secondary metabolites of plants whose basic structure consists of a 15 –carbon skeleton (C6-C3-C6), comprising of two 6-carbon benzene rings linked by a 3-carbon oxygen heterocyclic ring (Figure 1) [9]. Flavonoids can be classified into 12 subgroups based on the degree of oxidation of the

heterocyclic ring and the number of hydroxyl or methyl groups on the benzene ring. These subgroups include flavanones, flavones, isoflavones, chalcones, stilbenes, aurones, phlobaphenes, dihydroflavonols, flavonols, leucoanthocyanidins, proanthocyanidins, and anthocyanins [9]. Most of the plants from *Dodonaea* genus have been reported to contain flavonoids, the secondary metabolites which are responsible for a number of pharmacological activities associated with *Dodonaea* plant species.

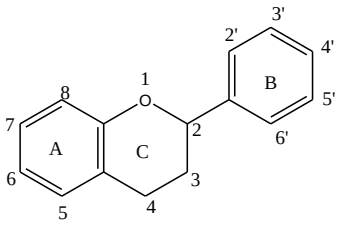


Figure 1: General structure of flavonoid

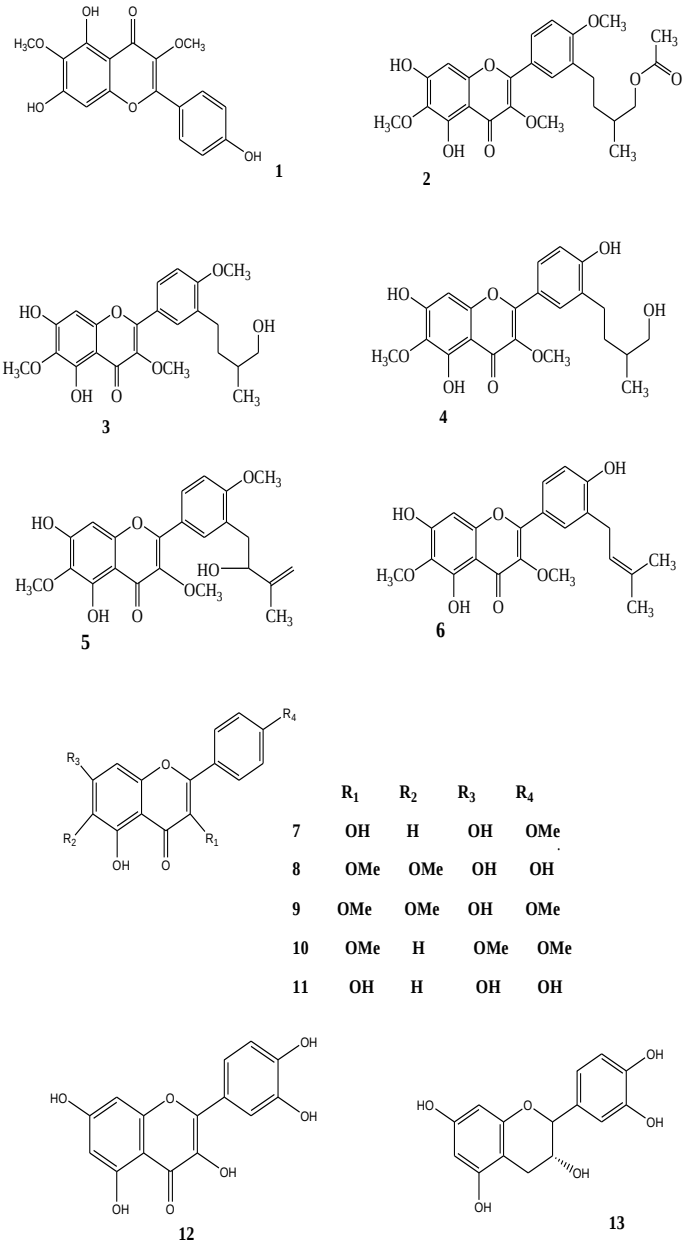
A number C-alkylated flavonoids have been reported as having been isolated from *Dodonaea viscosa*, including Viscosine (1) [10,11], 5,7-dihydroxy-3'-(4"-acetoxy-3"-methylbutyl)-3,6,4'-trimethoxy- flavone (2), 5,7-dihydroxy-3'-(3-hydroxymethyl-butyl)-3,6,4'-trimethoxyflavone (3), 5,7,4'-trihydroxy-3'-(3-hyroxymethylbutyl)-3,6-dimethoxy-flavone (4), 5,7-dihydroxy-3'-(2-hydroxy-3-methyl-3-butenyl)-3,6,4'-trimethoxyflavone (5), together with 5,7,4'-trihydroxy-3,6-dimethoxy-3'-isoprenyl-flavone (6) [12]. In another study, flavonoids related to kaempferol were purified from the dichloromethane and acetone fractions of *Dodonaea viscosa* [13]. They include 5, 7-trihydroxy-4'-methoxyflavone (7); 5, 7, 4'-trihydroxy-3, 6-dimethoxyflavone (8); 5, 7-dihydroxy-3, 6, 4'-trimethoxyflavone (santin) (9); and 5-hydroxy -3, 7, 4'-trimethoxyflavone (10) and 3,4',5,7-tetrahydroxy flavone (kaempferol) (11) [13]. In more recent but separate studies, 3,5,7,3′,4′-pentahydroxyflavone (12) [14] and 3,3′,4′,5,7-pentahydroxyflavane (13) [15] have been reported as having been isolated from the leaves of *Dodonaea viscosa*. The structures of these compounds are shown in figure 2.

Flavonoids have also been isolated from *Dodonaea angustifolia* (figure 3). In separate studies, 5-hydroxy-7,4′-dimethoxyflavone (14) [16], pinocembrin (15), santin (16), 5,7,4'-trihydroxy-3,6-dimethoxyflavone (17), and 5,6,7-trihydroxy-3,4'-dimethoxyflavone (18) [17] have been reported to have been isolated from the leaves of *Dodonaea angustifolia*. In another study, methylated flavonoids which included 5-hydroxy-3, 4′,7-trimethoxyflavone (19), and derivatives (20-26), were isolated from the leaves of *Dodonaea angustifolia* [8].

In recent studies, prenylated flavonoids bearing malonic acid moiety (figure 4) were reported as having been isolated from the leaves of *Dodonaea filiformis* and flowers of *Dodonaea spatulata* [18]. This sub-class of compounds has also been reported in *Dodonaea viscosa* [18-20]. Prenylation of flavonoids is thought to provide enhanced biological properties due to lipophilicity of the prenyl chains, which leads to higher affinity for biological membranes and enhanced interactions with target proteins [21]. This makes this subclass of flavonoids good at offering a wide range of pharmacological activities.

Terpenoids

Terpenoids are structurally diverse class of natural products derived from mevalonic acid and composed of several isoprene (5-carbons) structural units [22]. Based upon the number of isoprene units, these have mainly been classified into monoterpene (C10), sesquiterpene (C15), diterpene (C20), triterpene (C30), tetraterpene (C40), and polyterpene (C > 40) [22]. These subclasses of terpenoids may exist as hydrocarbons or as oxygen derived compounds such as alcohols, ethers and carbonyl compounds. In most plants, these compounds vary from those which are volatile to those which are non-volatile [23]. This class of natural products has also been reported in *Dodonaea* genus, and the compounds are thought to be responsible for a number of pharmacological properties exhibited by their various species.



	R_1	R_2	R_3	R_4
7	OH	H	OH	OMe
8	OMe	OMe	OH	OH
9	OMe	OMe	OH	OMe
10	OMe	H	OMe	OMe
11	OH	H	OH	OH

Figure 2: Flavonoids isolated from *Dodonaea viscosa*

A number terpenoids have been reported as having been isolated from *Dodonaea viscosa*, including diterpene, 6-hydroxy-5, 8, 9-trimethyl-18-carboxylclerodane (36) (Al Bimani and Hossain, 2020), clerodane-diterpene (37), two labdane diterpenes (38 and 39), labd-13(E)-en-8,15-diol and (40) ent-15,16-epoxy-9αH-labda-13(16),14-diene-3β,8α-diol (41) and 6-hydroxyhardwickjic acid (42) [24], tamarixetin, ent-labdane diterpenoids (43-50) (Gyeltshen, et al., 2023), ent-labdanes (51-58), ent-kauranes (59-62), Monoterpenoid wax esters (63-64) Viridiflorol (65) and Norhopene (66) [25]. Some terpenoid compounds isolated from *Dodonea* species are presented in figure 6 below.

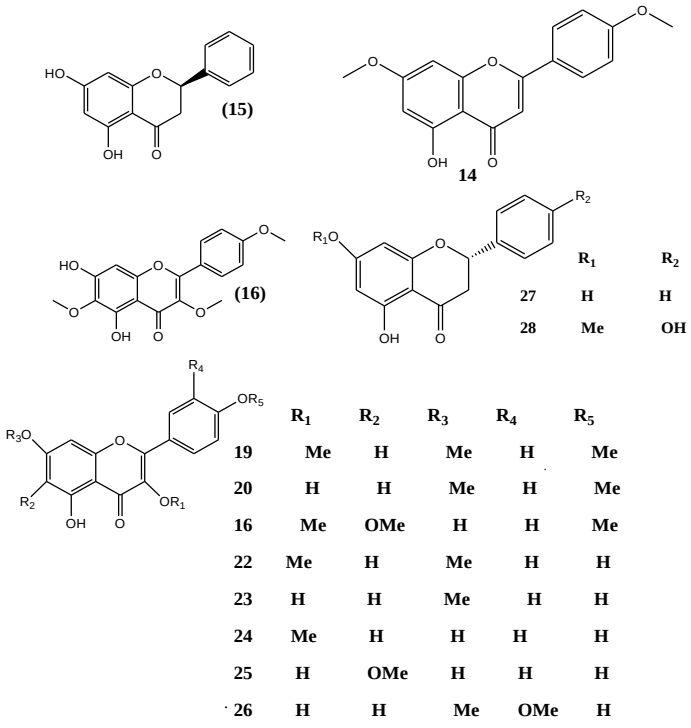


Figure 3: Flavonoids isolated from *Dodonaea angustifolia*

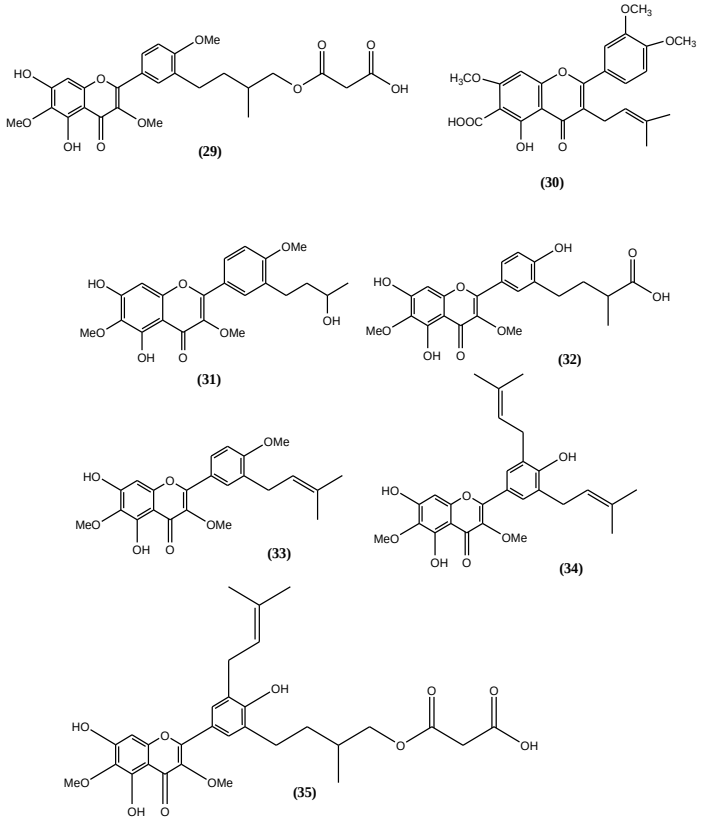


Figure 4: Prenylated flavonoids isolated from leaves of *Dodonaea filiformis* and flowers of *Dodonaea spatulate*

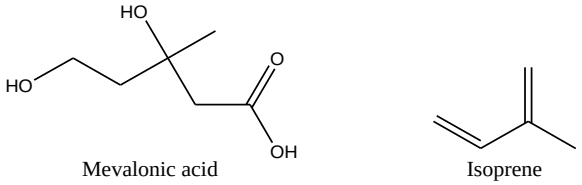


Figure 5: Structures of Mevalonic acid and Isoprene unit

Coumarins

Three coumarins: scopoletin (67), isofraxidin (68) and fraxetin (69) have been isolated from the stems of *Dodonaea viscosa*. (Sagara, et al., 2021). One other class of compounds predominantly reported among the *Dodonaea* species is glycosides.

Pharmacological Activities

Antioxidant

Methanolic extracts and the subsequent ethyl acetate and chloroform fractions of *Dodonaea* species have been reported to show good antioxidant capacity in research investigations using various in vitro assays including 1,1-Diphenyl-2-picrylhydrazyl (DPPH) scavenging assay, Ferric Reducing Antioxidant Power (FRAP) assay, and ferric thiocyanate assay, among others [15,20,26-30]. The antioxidant activity of these extracts has been associated with the presence of phenolic compounds such as flavonoids and coumarins in *Dodonaea* species [30]. In one study, 3,3′,4′,5,7-pentahydroxyflavane (13), a flavonoid isolated from the leaves of *Dodonaea viscosa* showed significant antioxidant activity against DPPH as compared to standard gallic acid [15]. In another study, 5-Hydroxy-7,3′4’-trimethoxy-6-acetoxy-3-prenylflavone (30) isolated from the leaves of *Dodonaea viscosa* also showed good antioxidant activity against DPPH [20].

Anti inflammatory

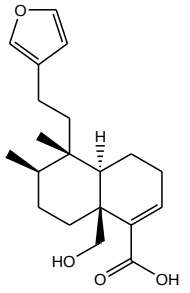
Plant extracts and even purified compounds from *Dodonaea* species have been reported to possess anti-inflammatory activities [31,32]. In one research study, crude extracts from powdered leaves of *Dodonaea viscosa* showed *in vivo* anti-inflammatory activity against carrageenan-induced rat paw edema at a dosage as low as 100mg/kg body weight [33]. In another study, an aqueous extract from the leaves of *Dodonaea angustifolia* formulated into silver nanoparticles inhibited in vitro anti-inflammatory effect against the denaturation of protein in a concentration dependent manner [34]. Other studies on in vitro anti-inflammatory activities of extracts from *Dodonaea* plants have also reported positive results [5,35,36]. Isolated compounds from *Dodonaea* plants such as Nebrodenside A, (glycoside) [37], Hautriwaic Acid (43) [38], among others have been reported to possess anti-inflammatory activities.

Antimicrobial

Plant extracts and pure compounds obtained from various *Dodonaea* species have been reported to possess good antimicrobial activities against various microorganisms including bacteria and fungi [13,16, 39-41]. In one study, crude extracts, fractions of ranging polarity and ensuing purified compounds (12 & 36) from the leaves of *Dodonaea viscosa* showed in vitro antimicrobial activity when assayed using agar diffusion technique [14]. In another study, compounds isolated from *Dodonaea angustifolia* were reported to possess good antibacterial and antifungal activity [8,16]. Many other compounds, fractions and crude extracts have reported good antimicrobial activity.

Antiplasmodial

Pinocembrin (15) and three other compounds isolated from the leaves of *Dodonaea angustifolia* were reported to possess significant antiplasmodial activities [17]. Another study reported a significant *in vivo* antiplasmodial activity of methanolic extract and its subsequent different polarity fractions obtained from the roots of *Dodonaea*



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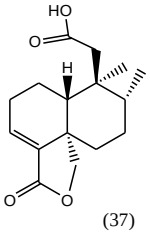

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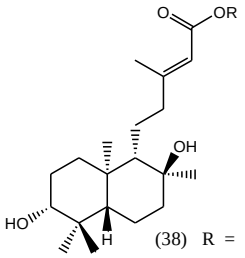
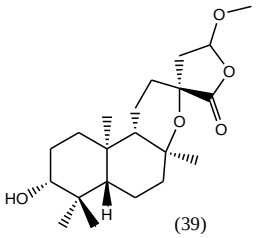


(38) R = H



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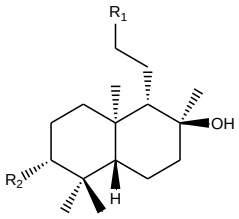

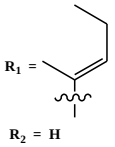

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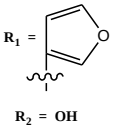

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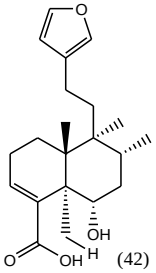

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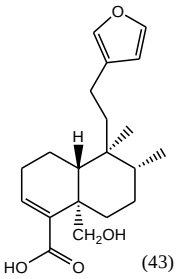

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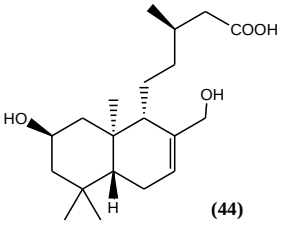

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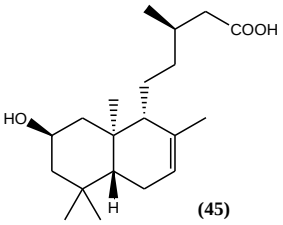

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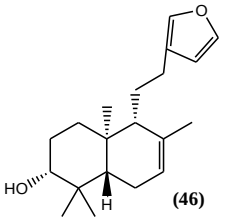

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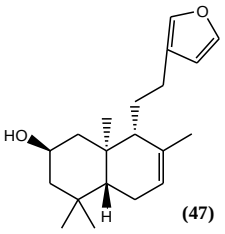

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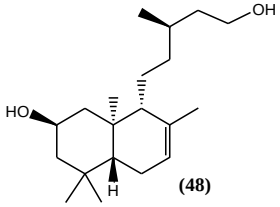

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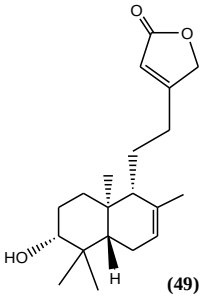

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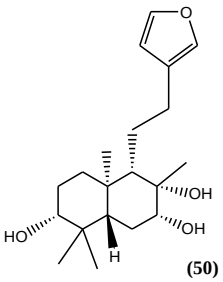

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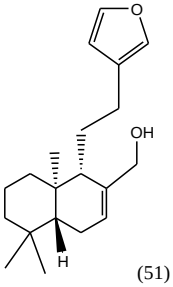

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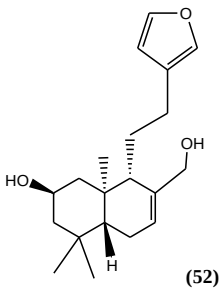

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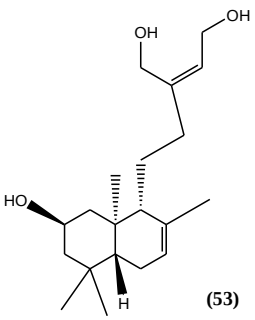

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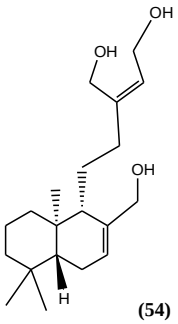

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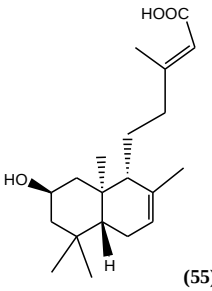

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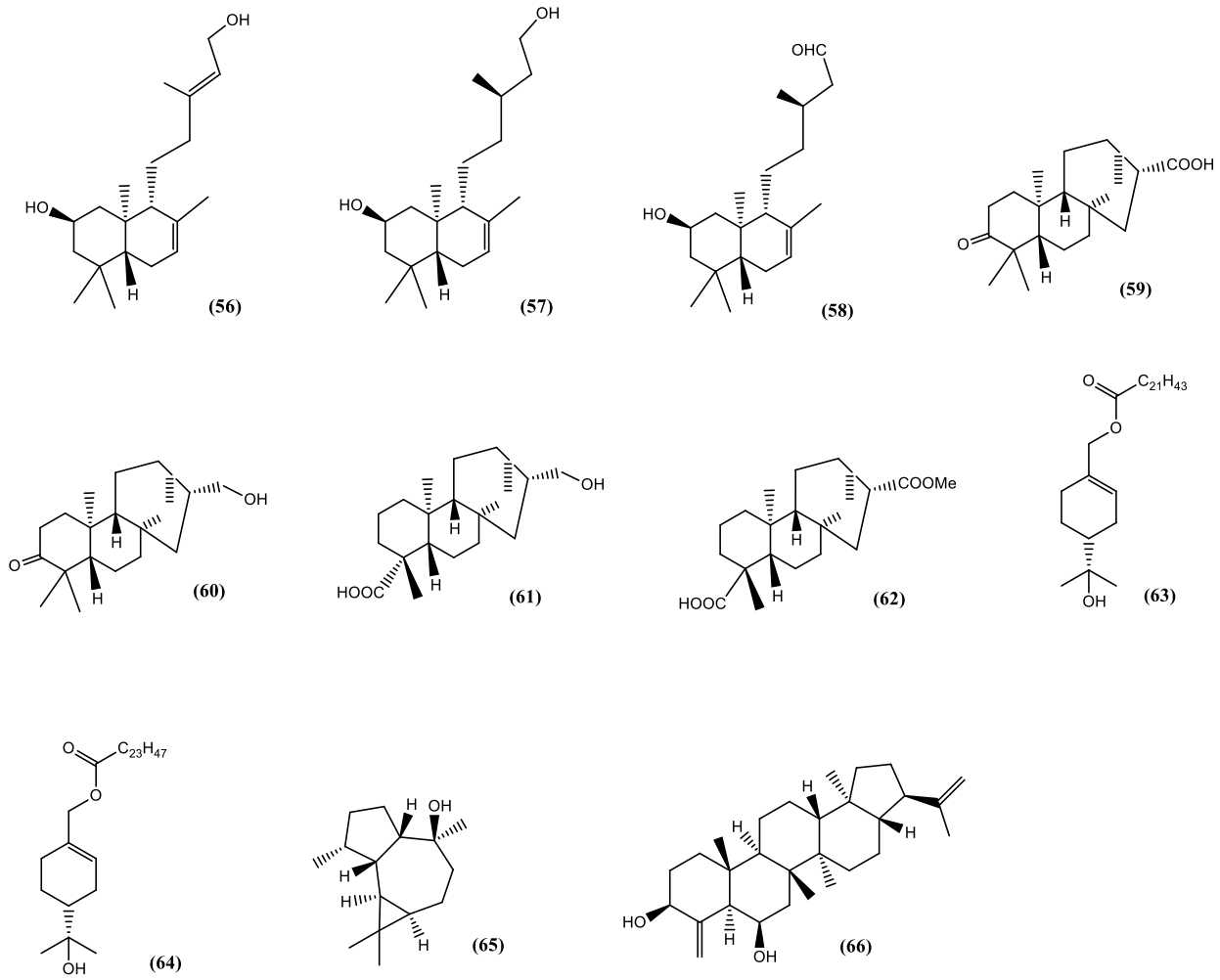
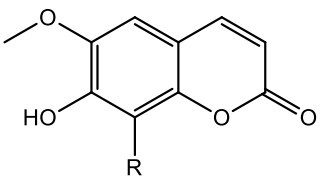


Figure 6: Terpenoids isolated from *Dodonaea* species

angustifolia [42]. A seed extract of *Dodonaea angustifolia* has also been reported to show *in vivo* activity against *P. berghei* in mice [43]. Other studies have reported potential of *Dodonaea* species' application in management of plasmodium infections [1,44].

Other Pharmacological Activities

The other reported pharmacological activities possessed by *Dodonaea* species include anticancer [1,45], antiviral [1,46-48] and antidiabetic [1,49], among others.



(67) R = H
(68) R = OCH_3
(69) R = OH

Figure 7: Coumarins isolated from *Dodonaea viscosa*

CONCLUSION

In conclusion, *Dodonaea* species contain various phytochemicals such as flavonoids, terpenoids, coumarins and glycosides, among others. These photochemicals are thought to be responsible for the various pharmacological activities the plant species possess. Extracts from various species of *Dodonaea* plants have been reported to possess a range of activities including but not limited to antioxidant, anti-inflammatory, antimicrobial, antiplasmodial, anticancer, antidiabetic and antiviral activities.

Conflicts of Interest

The authors declare no conflict of interest.

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