

DURANTA REPENS LINN. (VERBENACEAE): A COMPREHENSIVE REVIEW OF PHARMACOGNOSTIC, ETHNOMEDICINAL, PHARMACOLOGICAL, AND PHYTOCHEMICAL ASPECTS

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ABSTRACT

Objective: This review is intended to investigate the published report regarding phytochemical, ethnomedicinal, and pharmacological activities and put forth the therapeutic potential of *Duranta repens* Linn. (*D. repens*). It belongs to the family *Verbenaceae*, one of the therapeutically important plants, broadly distributed all throughout the world. It is commonly referred as golden dewdrop, angel whisper, pigeon berry, or skyflower.

Methods: I utilized logical writing and scientific literature regarding *D. repens* by referring search engine such as Springerlink, ScienceDirect, SciFinder, PubMed, Scopus, Google Scholar, and BioMed Central as well as relevant books, websites, scientific publications, and dissertations as a source of information that provided an up-to-date review. My work on morphology and extraction of various phytochemicals and their evaluation has helped to provide an insightful account of *D. repens*.

Results: Phytochemical profiling of these species revealed the presence of some imperative phytochemicals such as alkaloids, flavonoids, glycosides, phenolics, saponins, steroids, tannins and terpenoids as the basis of its valuable therapeutic properties. The other imperative phytoconstituents which contribute to the therapeutic properties are durantol, repennoside, repenins, and scutellarein. The pharmacological activities exhibited by *D. repens* as antimicrobial, antioxidant, and insecticide properties are attributed to the presence of valuable bioactive phytoconstituents.

Conclusion: Considering these facts, I endeavored to present a comprehensive review enlightening the phytochemistry and pharmacological activities of plant *D. repens*. Future research can be directed to an extensive investigation about phytochemistry, clinical trials, pharmacokinetics, and acquiring safety data so as to add new dimensions to the therapeutic utilization of *D. repens* and other *Duranta* species.

Keywords: *Duranta repens*, *Verbenaceae*, Microscopical characters, Phytochemicals.

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INTRODUCTION

Duranta repens Linn. (*D. repens*) belonging to family *Verbenaceae* is native to clean and open forests. It is used as an ornamental plant in tropical nations [1,2]. The genus *Duranta* was described by Linnaeus (1753). This genus is named after Castor Durante (1529–1590), a French physician and botanist [3]. The plants of *Verbenaceae* family are herbs, shrubs, or trees comprising about 100 genera and 2,600 species. Around 35 *Duranta* species with evergreen bushes are spread over tropical and subtropical areas. *D. repens* was used in Egypt as an ornamental plant [4]. *D. repens* (Golden dewdrop) otherwise called sky blossom, angels-whisper, additionally called Katamehedi. *Duranta* is an upright to hanging bush that occasionally takes the type of a scrambling bush or once in a while a little tree [5,6]. They mostly occur in tropical and subtropical and few temperate regions. Habit varies from tree lianas to shrubs and herbs. Leaves are simple, opposite or alternate arranged, entire or divided, and exstipulate. Flowers are often involucre of colored bracts. Plants are sometimes thorny. Fruits are fleshy drupes, usually 8-seeded, completely enclosed by the persistent calyx. Fruits are less commonly capsular or schizocarps. Seeds show a presence of oily embryo with little or absence of endosperm. The economic uses include as sources of timbers, essential oils, teas, herbal medicines, fruits, gums, tannins, and ornamentals. Flowers are small mostly blue–purple, or white bracteates with racemes are either terminal or axillary. Calyx tube subcampanulate ribbed and toothed. Corolla tube is cylindrical straight or apically curved and pubescent at the mouth. An Ovary is 4-carpelled with 8 locules, one ovule in each lobule, style terminal with unequally 4-lobed stigma [7,8].

Introduction to *D. repens*

Taxonomical classification [9,10]

Domain: Eukaryota
 Kingdom: Plantae
 Subkingdom: Tracheobionta (Vascular plants)
 Phylum: Spermatophyta
 Subphylum: Angiospermae
 Class: Dicotyledonous
 Subclass: Asteridae
 Order: Lamiales
 Family: *Verbenaceae* (the Vervain family)
 Genus: *Duranta*
 Species: *Duranta repens*
 Common Name: Golden Dewdrop

Vernacular names[11]

English: Golden dewdrop, pigeonberry, and skyflower
 Kannada: Neelakantha
 Marathi: Piwali Mendi
 French: Vanillier de Cayenne
 Indonesian: Sinyo nakal
 Japanese: Taiwan-rengyô
 Tongan: Mavaetangi
 Vietnamese: Thanhquan
 South Africa: Geelbessi

GEOGRAPHIC DISTRIBUTION OF *D. REPENS*

Golden dewdrop grows wild mostly in a dry coastal area from near sea level to over 100 m in elevation. It grows in areas with moister habitat, and especially, along roads. Golden dewdrop is native to Mexico, Central America, South America Argentina, Southern Florida (possibly naturalized), Bermuda, the Bahamas, and the West Indies. The species is widely cultivated in tropical and subtropical regions which includes Hawaii, American Samoa, and Guam. It is extensively cultivated throughout India along the sides of rivers and banks of streams. It grows on rocky slopes and mostly found sometimes along roadsides in villages [12-16]. Golden dewdrop forms a part of the coastal scrub community and contributes to soil and ecosystem stability. It is a commonly grown plant when trimmed forms a strong, compact hedge which is almost impenetrable to cattle. It is a popular ornamental plant used as an accent and planted in tropical and subtropical parts of the world because of its profuse displays of flowers [17].

TRADITIONAL USES OF *D. REPENS*

Traditional plants are an important source of a natural remedies and remain to be broadly used to treat many diseases [18]. An infusion of the leaf and juice of the fruit is diuretic, and flower is said to have stimulant properties. Both leaf and fruit give a positive test for hydrocyanic acid. In the Chinese system of medicine, fruits are mentioned as poisonous berries. The plant is claimed to treat malaria which still stands as a major disease in the developing countries. Water-macerated fruits yield a juice which even in dilutions of 1:100 parts of water are lethal to mosquito larvae; the action is less marked on culicine larvae. The juice can be used as a larvicidal in ponds and swamps. Fruit contains an alkaloid analogous to narcotine while leaf contains saponins. Some glycosides are also reported from the bark of the plant. In Chinese medicine, the fruits were used for the treatment of malaria, and the leaves are employed for the treatment of abscesses [19]. The fruit is said to cause illness and death in children. The symptoms imply sleepiness, high temperature, dilated pupil, rapid pubes, swelling lips and eyelids, and convulsions [20]. The seeds yield oil with the following characteristics: Acid value (58.62%), saponification value (210.9), iodine value (101.3), and unsaponifiable matter (0.4%) [21]. The plant is believed to be poisoning the livestock and is said to be very bitter hence not eaten by livestock [22].

CHARACTERISTICS OF THE PLANT *D. REPENS*

The shrub grows up to a 7 m with branches subquadrangular, drooping or trailing, spiny, and sparsely pubescent and turns glabrous with age. Terminal inflorescence is axillary with 10-30 cm long and racemed with many flowers. It is usually erect recurved with 3-10 cm long pubescent. A peduncle of the flower is 5-15 mm longer in size. Flowers have a fragrance with minute bracts. They are linear 1-4 mm long with lower ones occasionally subfoliaceous exceeding the calyx. The pedicel is 1-5 mm long and pubescent shown in Fig. 1.

Calyx is long 3-7 mm tubular glabrescent with appressed pubescent or canescent outside. It is glabrous inside with 5-angled tube and 5-min teeth at the rim. The base is triangular, and the apex is subulate about 0.5-1 mm long. Corolla is light bluish-purple or white in color. It is puberulous outside, pubescent inside, often glandular with tube 6-10 mm long and 1.5-2 mm diameter. Stamens inserted above the middle of the corolla-tube are filaments with 0.5-1.5 mm long and appear with few hairs. Anthers are oblong and ± 1 mm long. Ovary is subglobose glabrous with style 2-3 mm long stigma is minutely capitate and 4-lobed. Fruit is orange-yellow with subglobose or obpyriform and glabrous completely enclosed by the accrescent orange-yellow shiny calyx. Macroscopical characters of the leaves as shown in Fig. 2 demonstrate a dark green color on both surfaces seen as deciduous; leaf base is decurrent symmetrical petiolated.

The composition of the lamina is simple, pinnate reticulate venation, entire margin, acuminate apex, sub-ribs alternate, surface glabrous, and texture subcoriaceous. The size of leaves varies from 1.5 to 4.6 cm in length and 2.4 cm in breath [23]. *D. repens* shows several stems or

drooping spiny branches, especially when carrying a large number of fruit. The bark is light gray, becoming rough, and fissured when old. There are usually at least some pairs of spines along the stems, one located at the base of each of the leaf stalks [24].

BIOLOGICAL AND PHARMACOLOGICAL ACTIVITIES

Natural products have been playing a substantial part throughout the world in treating and averting human diseases [25]. Literature proposes that *D. repens* L. has been accounted for a wide variety of medicinal activities. The whole plant is used in the treatment of infertility, pneumonia, and malaria, as diuretic, itches, anthelmintic, neuralgic disorders and also as an insect repellent. *D. repens* also exhibits activities such as anti-shigellosis, cytotoxic potency, antiviral activity, antioxidant, antibacterial, and antimicrobial against human pathogens [24-29] (Table 1).

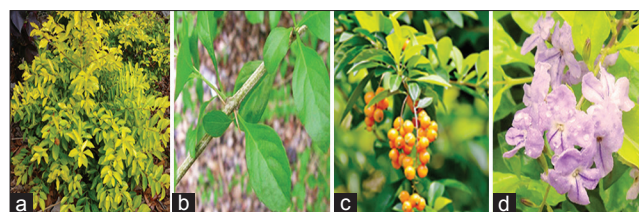


Fig 1: Morphology of the *D. repens* Linn. Plant. (a) Plant of *D. repens* L. (b) Stem of *D. repens* L. (c) Fruits of *D. repens* L. (d) Flower of *D. repens* L.

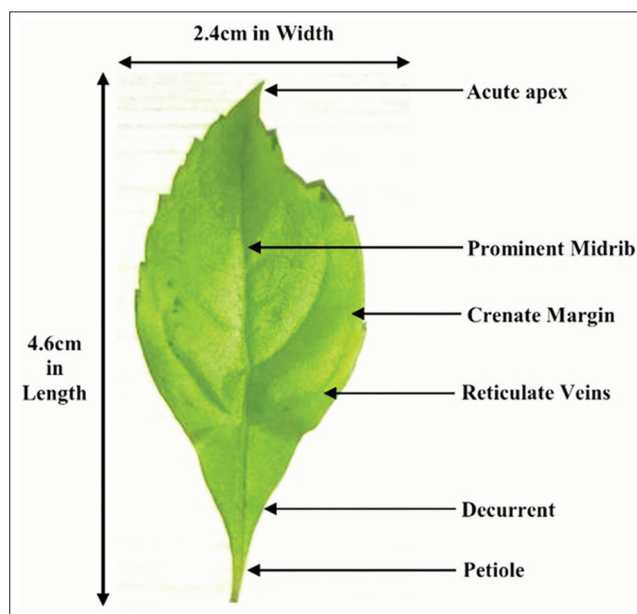


Fig. 2: Macroscopical characteristics of *Duranta repens* Linn. leaf

Table 1: Biological activities of *D. repens*

Sr. No	Activity reported	Reference
1	Thrombin inhibitory	[30,31]
2	Mosquitocidal	[41]
3	Antiviral	[33]
4	Cytotoxicity	[32]
5	Antioxidant	[45-47]
6	Antiplasmodial	[39]
7	Anti-shigellosis	[34]
8	Antifungal	[37,38]
9	Antimicrobial	[34-36]
10	Insecticidal Property	[42-44]

D. repens: *Duranta repens*

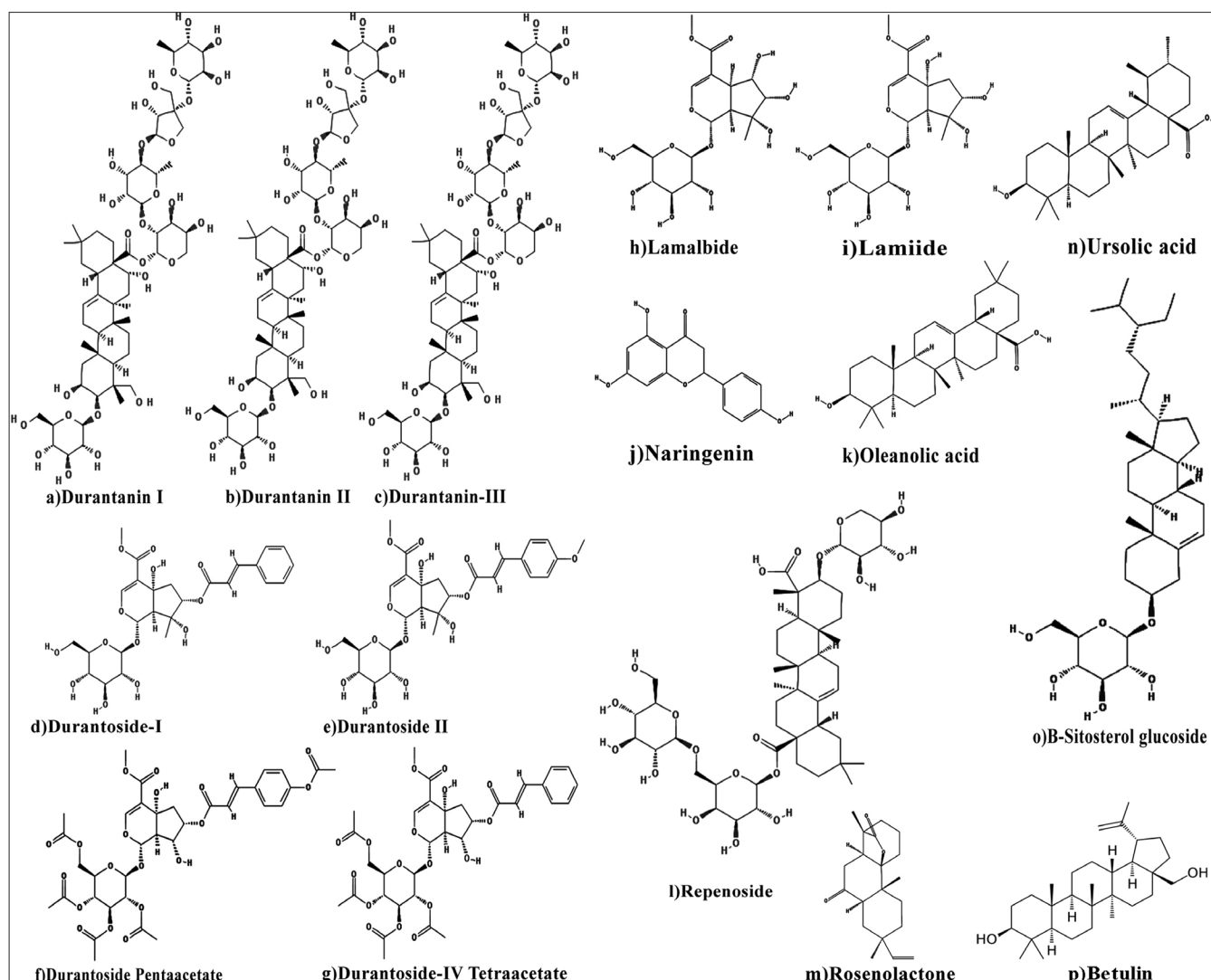


Fig. 3: Phytoconstituents of *D. repens* Linn.

Thrombin Inhibitory Activity

Anis *et al.* reported isolation and evaluation of isoprenylated flavonoids, tri-methoxyflavone, isoprenylated acetophenone, and other derivatives for thrombin inhibitory activity. Results concluded inhibitory activity against propyl endopeptidase active against thrombin [30]. Anis *et al.* isolated C-alkylated flavonoids, trans-clerodane diterpenoids, and other constituents from *D. repens*. The known flavonoid was reported for the first time from this species. This flavonoids showed significant thrombin inhibitory activity [31].

Cytotoxic activity

Ahmed *et al.* isolated two new triterpene saponins and ten known compounds and screened for cytotoxic activity on brine shrimps. The investigated methanol extract and compounds, durantin, known as compound 2 and 7 showed significant cytotoxic activity against a HepG2 cell line [32].

Antiviral activity

Abou-Setta *et al.* reported antiviral activity of the ethanolic extract of *D. repens* against hepatitis A virus. Results showed 76% reduction in viral titer of hepatitis A with ethanolic extract at the concentration of 40 µg/mL, while at 20 µg/mL, the inhibition reached 64% determined by plaque reduction assay. The methanolic extract showed 88% inhibition at the concentration of 40 µg/mL, while at 20 µg/mL, the inhibition reached 59% of the virus by the same assay. They suggested

that this antiviral activity may be attributed to the acetosides or lamiide content of the extract [33].

Antimicrobial activity

Nikkon *et al.* reported extraction, fractionation, and isolation of two triterpenes (β -Amyrin and 12-Oleanene) from the chloroform-soluble fraction of an ethanolic extract and also determined minimum inhibitory concentrations (MIC) of the ethanolic extract of *D. repens* stem, which were evaluated for antibacterial and antifungal activities by the disc diffusion method and cytotoxicity by brine shrimp lethality bioassay. The MICs of the extracts (stem and fruits), their fractions, and compound 1 were found to be in the range of 32~128 µg/ml [34]. Ogbuagu *et al.* evaluated the antibacterial activity of methanolic extract obtained from Nigerian *D. repens* leaves against some human pathogenic bacteria: *Proteus mirabilis*, *Bacillus subtilis*, *Salmonella typhi*, and *Boletus aereus* at 75, 150, 300, and 600 mg/mL by the agar diffusion method. The result of MIC determined showed significant activities against the growth of *P. mirabilis*, *B. subtilis* (141 mg/mL), *S. typhi* (81 mg/mL), and *B. aereus* (100 mg/mL) [35]. Jayalakshmi *et al.* reported the antibacterial activity of various solvent extracts of medicinal plants against the human pathogenic bacteria such as *Escherichia coli*, *Klebsiella pneumoniae*, *B. subtilis*, *Bacillus cereus*, *S. typhi*, *E. aerogenes*, and *S. aureus* by agar cup diffusion method. Methanol extracts of *D. repens* L. showed significant antibacterial activity. The antibacterial activity of plant extract is promising as compared to standard drugs streptomycin and gentamicin [36].

Antifungal activity

Sharma *et al.* reported the antifungal properties of the methanolic extract of different parts such as leaves, stem, and roots of *D. repenes* against *Aspergillus niger*, *Aspergillus flavus*, *Aspergillus umigatus*, and *Penicillium sp.* using agar disc diffusion method. They reported that methanolic extract of leaf and stem of *D. repenes* was effective against *A. niger*, *A. flavus*, and *A. fumigatus* at 1000 mg/mL concentration which recorded significant inhibition zone of 2.3 cm, 2.3 cm, and 2.2 cm, respectively [37]. Sikarwar *et al.* investigated the antifungal activity of aqueous and methanolic leaf extracts of *D. repenes* against three fungi *A. niger*, *C. albicans*, and *M. gypseum* by disc diffusion method. The result showed promising antifungal activity against the tested fungi. Antifungal activity of the test extracts at different inhibitory concentration varied significantly (0.05 level of significance). Where methanolic extract proved to be effective compared to the aqueous one [38].

Antiparasitic activity

Ijaz *et al.* reported that *D. repenes* from Pakistan showed antiplasmodial activity against the chloroquine-sensitive and chloroquine-resistant strains of *Plasmodium falciparum*, with IC_{50} values of 8.5 ± 0.9 and 10.2 ± 1.5 $\mu\text{g/mL}$, respectively [39].

Insecticidal property

El-Naggar and Mosallam evaluated that extracts from *D. repenes* had antifeedant and insecticidal properties against the larvae of *Culex pipiens* and *Spodoptera littoralis* and the adults of *Musca domestica* [40]. Nikkon *et al.* reported larvicidal activity of crude extracts from the stem and fruits, and their fractions and fresh fruit juice of *D. repenes* were assayed against the larvae of *Culex quinquefasciatus*. The highest larval mortality was found in chloroform-soluble fraction of the stem, with 12 h- LC_{50} being 10.75 ppm, and in ethanolic extract of fruits, with 12 h- LC_{50} being 8.51 ppm against the first instar larvae. Various concentrations of fresh fruit juice showed potent effects on *C. quinquefasciatus*, and the larvae showed proportional tolerance with the increase of their age and time. These results suggest that the stem and fruits of *D. repenes* are very effective natural larvicidal and can be useful against *Culex quinquefasciatus* [41]. McConnell *et al.* evaluated insecticidal property of the methanol and water extracts of *D. repenes* Linn. leaves against larvae of *C. quinquefasciatus* (Say). Here, both the extracts of *D. erecta* have larvicidal activity [42]. Hemavathy *et al.* reported larvicidal activity of the aqueous and methanolic extracts of *D. repenes* leaves from India against larvae of *C. quinquefasciatus* that showed the high percentage of mortality compared to ethanolic extract. At 10% concentration of the extract of water, methanol, and ethanol, the larvae found to be dead were 17, 16, and 13 of 20 larvae [43]. Roy *et al.* evaluated an aqueous extract of *D. repenes* from India against the teared spider mite (*Oligonychus coffeae*) to determine its effect on adult mortality, the viability of eggs, oviposition deterrence, and repellent properties. The direct spray method was used at concentrations of 2, 4, 6, 8, and 10 g/L. Deposition of eggs by adult mites on treated leaf surfaces decreased, and the viability of eggs was also reduced. Its efficacy was comparable to that of the commonly used commercial neem oil azadirachtin formulation. In addition, in the field, the application of the aqueous extract of *D. repenes* reduced the mite population, and its efficacy was comparable to that of the synthetic pesticide propargate [44].

Antioxidant activity

Ahmad *et al.* reported phytochemical investigations on the chloroform-soluble fraction of the whole plant of *D. repenes* Linn. They isolated four new coumarinolignoids: Repenins, coumarinolignoids, cleomiscosin, and durantin. The compounds showed significant radical scavenging activity against 2,2-diphenyl-1-picryl-hydrazyl-hydrate (DPPH) radicals, with IC_{50} values in the range 0.420–0.625 mM. Repenin displayed the strongest scavenging potential with IC_{50} values of 0.420 mM [45]. Shahat *et al.* isolated three compounds from methanol extract of *D. repenes* from Egypt, i.e., phenylethanoid glycoside, acetosides, iridoid lamiide, and saponin pseudo-ginsenoside-RT1. Acetosides showed an

IC_{50} of 3.05 ± 0.09 $\mu\text{g/mL}$ in the DPPH assay, while lamiide and pseudo-ginsenoside-RT1 were not active [46]. Khan *et al.* investigated ethanol and methanol extracts of *D. repenes* fruits for the antioxidative potential that can protect H_2O_2 -induced oxidative cell damage. HEK293T cells were treated with different concentrations (0–1000 $\mu\text{g/mL}$) of ethanol extract and methanol extract of *D. repenes* for 24 h and then treated with 100 μM H_2O_2 for 24 h. They determined cell viability and antioxidant constituent of the extracts. Treatment with a limited dose of both extracts increased the survival rate of H_2O_2 -treated HEK293T cells; however, the extra-high dose showed growth inhibitory effect. The results showed treatment with both extracts protected cellular lipid peroxidation. *In vitro* analysis showed that ethanol and methanol extracts increased the survival rate of H_2O_2 -treated HEK293T cells, lipid peroxidation, 2, 2-diphenyl-1-picrylhydrazyl, and H_2O_2 scavenging activities. A limited dose of ethanol and methanol extracts possesses antioxidative potential, which can protect H_2O_2 -induced oxidative cell damage [47].

Phytochemical composition

Literature proposes that *D. repenes* L. contains a wide array of various bioactive compounds. Interestingly almost all parts of the *D. repenes* species have been exploited for phytochemical investigation, and various phytoconstituents are isolated till date. Various important phytoconstituents have been reported such as C-alkylated flavonoids, steroids, flavonoids, terpenoids, triterpenes, beta-sitosterol, naringenin, triterpenes saponins, steroidal glycosides, and glycosides as shown in Fig. 3. From *Duranta* genus, several iridoid glycosides as durantosides are isolated. The leaves contain a saponin, and fruits contain alkaloid analogous to narcotine [48]. Itrat *et al.* 2001 reported the two C-alkylated flavonoids, two C-tropane type of triterpenes, and flavonoid as 3,5,4'-trihydroxy-6,7-dimethoxyflavone [49]. Ahmed *et al.* from the chloroform fraction of *D. repenes* isolated 24-ethyl-25-hydroxycholesta-4,22(23)-dien-3-one steroid [50]. Harbome *et al.* reported a 5,6,7-trihydroxy-4'-methoxy-flavone [51]. Kuo *et al.* described a new iridoid, durantoside-IV pentaacetate from the leaves of *D. repenes*. The same authors, working on the leaves of this plant, recently reported oleanolic and ursolic acids and from the hexane extract β -sitosterol glucosides. From the acetone extract, they have also reported inorganic salts from the water-soluble portion of ethanolic extract and E-cinnamic acid, and (E)-p-methoxycinnamic acid and a fraction containing a strongly bitter substance were isolated from the ethyl acetate soluble fraction of the ethanolic extract. The fraction containing bitter substances was later found to comprise of glucose pentaacetate, kusagin non-acetate, and verbascoside [52–56]. Hiradate *et al.* reported three triterpenoid saponins, durantin-I, II, and III, respectively, from the leaves of *D. repenes* which are the plant growth inhibitors. Durantoside-I pentaacetate, durantoside-I tetraacetate, durantoside-II tetraacetate, durantoside-IV pentaacetate, and durantoside-V tetraacetate were also isolated from *D. repenes* [57,58]. Rimpler and Timm reported the presence of three iridoid glucosides as durantoside-I, II, and III [59]. Rao *et al.* reported durantoside-IV [60]. Other constituents reported were (+)-Hardwickiic acid [61], (+)-3,13-Clerodadien-16,15-olid-18-oic acid [62], betulin [63], stigmaterol [64], stigmaterol 3-O-,8-D-glucopyranoside [65], andscutellarein and pectolarigenin [66].

CONCLUSION

Based on the existing review of literature, *D. repenes* reveals its valuable therapeutic use as antimicrobial, antifungal, antiviral, and antimalarial and in other parasite infestation. It has a potent free radical scavenging activity which sufficiently demonstrated in different experimental and clinical studies. Its potential as an antioxidant and cytoprotective agent needs to be undermined in future research work. Various unique molecules of *D. repenes* can also be chemically modified or used as "lead" for developing more effective drug molecules. Therefore, extensive pharmacological and phytochemical analysis, experimentations, together with pharmacokinetic and toxicological studies will be a focus for

forthcoming investigation. Furthermore, a well-designed study to measure its toxicity from its long-term use is another urgency. This review article emphasizes the potential of *D. repens* that can be employed in new therapeutic drugs and will offer the base for future research on the application of herbal medicines.

AUTHORS' CONTRIBUTION

Abhijeet Puri: Concept of paper, compiling full literature, the inscription of a manuscript, revising, the read-through of the manuscript, and contributed to improve the standard of the manuscript.

CONFLICTS OF INTEREST

The authors declare that he has no conflicts of interest.

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