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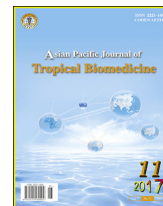
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### An updated review on pharmacological activities and phytochemical constituents of evening primrose (genus *Oenothera*)



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#### ABSTRACT

Genus *Oenothera* includes medicinal plants that are distributed throughout the world and are known since ancient times. Popular indications of different species of this genus include treatment of inflammations, diabetes, microbial infections, ulcers, tumors, kidney and liver problems. The plants of this genus are a botanical source for various pharmaceutically active components like sterols, alkaloids, phenolic acids, flavonoids, triterpenoids, saponins, biflavonols and tocopherols. This review article is a compilation of chemical composition and biological activities of the various species of the genus *Oenothera*.

## 1. Introduction

Herbal plants play a significant role in the life of humans as they are being used in different fields such as pharmacology, cosmetics, perfumery, nutraceuticals, beverages and dying industries. Years ago, before the development of synthetic drugs, these herbs were mainly used as an alternative therapy to treat various kinds of diseases. *Oenothera*, belonging to family Onagraceae, is the second largest genus with 145 species of flowering plants [1]. It mainly occurs in temperate America as well as in tropics. The genus is commonly recognized as evening primrose family that consists of herbs and under shrubs. The plants of this genus occur in the form of annual, biennial or perennial herbs with alternate and mostly narrow leaves. The species of *Oenothera* are known for their saucer-

shaped white, pink, yellow and red flowers, and most are fragrant [2].

The plants owned to *Oenothera* have a wide range of medicinal properties that prompted us to compile a review article on this particular genus. It comprises all the currently available literature related to the pharmacological activities and phytochemical constituents of the different species of *Oenothera* including some of the findings of our own research work [3].

## 2. Pharmacological activities

### 2.1. Antioxidant activity

Antioxidants play an important role in the preclusion of human diseases. Medicinal plant is a rich source of natural radical scavengers and it is believed that this radical scavenging property is the main causative factor to the therapeutic assistance of many medicinal plants. As far as antioxidant capacity of genus *Oenothera* is concerned, it dates back to the mid of 90s. One of its member *Oenothera biennis* (*O. biennis*) L. is the most important medicinal plant. In year 1995, its antioxidant property was reported for the first time using lard as the substrate. Antioxidant power was assessed based on measuring peroxide

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number of the sample. Research showed that ethanolic extract of *O. biennis* L. exhibited pronounced antioxidant activity [4,5]. Years later, it was explored that the triterpenoids found in methanol/water extract of *O. biennis* also have the potential of radical scavenging activity [6]. In year 2006, the lipophilic triterpenoidal esters present in cold-pressed, non-raffinated evening primrose oil were found to be effective in reducing oxidation stress [7]. The pressing residues from *O. biennis* were also reported to possess a very high antioxidant property [8]. In year 2009, methanolic extract of the seeds of *O. biennis* were also investigated using DPPH and were found to possess significant radical scavenging activity [9]. A research carried out in 2010 showed that *O. biennis* is one of the most common botanicals used in anti-aging creams due to its antioxidant properties [10]. In the same year, the aerial parts of *Oenothera speciosa* (*O. speciosa*) Nutt were also explored for the determination of their antioxidant potential. It was found that 80% methanolic extract of *O. speciosa* showed potent *in vitro* antioxidant activity using DPPH radical assay [11].

*Oenothera paradoxa* (*O. paradoxa*) is also an active member of genus *Oenothera*. An experiment was conducted on three different extracts of defatted seeds of *O. paradoxa* Hudziok, 60% ethanolic extract, aqueous extract, and 30% isopropanolic extract, differing by their total content of phenolic compounds and contents of individual polyphenols. It was found that the 60% ethanolic extract exhibited most promising antioxidant activity due to its greater total content of phenolic compounds and higher content of pentagalloyloglucose [12].

In year 2013, another member of this genus *O. paradoxa* Hudziok was found to protect the skin from any UVA induced damage [13].

The radical-scavenging capacity of oil seed cake extracts of *O. biennis* was evaluated against 2,2-azinobis (3-ethylbenzothiazoline-6-sulphonic acid). Research showed that the alcoholic extract of oil seed cakes exhibited strong antioxidant capacity [14,15]. The antioxidant capacity of the roots of *O. biennis* was also evaluated against DPPH and was found to possess high antioxidant potential [16].

In a study conducted in year 2015, *in vivo* and *ex vivo* properties of emulsions of *O. biennis* seedcake extracts were evaluated using the tewameter, pH meter, corneometer, methyl nicotinate model of micro-inflammation in human skin, and tape stripping of the stratum corneum. The studies exhibited that the emulsions with *O. biennis* seedcake extracts have strong anti-inflammatory and antioxidant activity [17].

By using melan-A cells, *in vitro* antioxidant and anti-melanogenic effects of methanolic extract of *Oenothera laciniata* (*O. laciniata*) was investigated using 3-ethylbenzothiazoline-6-sulphonic acid radical-scavenging and superoxide dismutase assays. The methanolic extract showed a good antioxidant activity and anti-melanogenic effect in melan-a cells that was superior to that of arbutin, a well-known skin-whitening agent [18].

## 2.2. Anti-diabetic activity

The rapidly increasing diabetes mellitus is becoming a serious intimidation to human health all over the world. Several treatments are available to control diabetes, but no perfect remedy has been reported yet. The herbal medicines are thought to provide a better treatment against diabetes through improving the immunity of the body.

In 2003, a study was conducted on rats to determine the activity of ethanolic extract from defatted seeds of evening primrose *O. biennis* L., to control the rise of blood glucose level. It was found that the extract played an imperative role in the suppression of postprandial hyperglycemia [19]. An investigation on the antidiabetic activity of *Oenothera erythrosepala* Borb was also carried out in the very next year. It was reported that the dose of 15 g/100 mL of the oil of *Oenothera erythrosepala* Borb can lower the fasting blood glucose in experimental animals [20].

Few years later, the anti-hyperglycemic activity of aerial parts (leaves and stems) of *O. speciosa* Nutt was also investigated by conducting an experiment on rats. It was concluded that 80% aqueous methanolic extract exhibited momentous anti-hyperglycemic activities in dose dependant manner [21].

In year 2015, a study was conducted on some edible plants including *O. paradoxa* to investigate their antidiabetic activity. Their polyphenolic extracts were screened in terms of  $\alpha$ -amylase,  $\alpha$ -glucosidase and protein tyrosine phosphatase 1B inhibitors. The study concludes that among these plants *O. paradoxa* may be considered as a promising natural source for active compounds with antidiabetic properties [22].

## 2.3. Anti-inflammatory activity

Complementary and alternative medicine, particularly herbal therapy, is generally used by the patients with inflammatory diseases. In 2004, the anti-inflammatory activity of methanolic extract of *Oenothera rosea* (*O. rosea*) was determined for the first time by carrageenan-induced rat paw edema model. It was found that 70% of the plant extract of *O. rosea* produced a high reduction of edema [23]. Later on, the aerial parts (leaves and stems) of *O. speciosa* Nutt were also reported to possess *O. speciosa* Nutt significant anti-inflammatory activities in a dose dependant manner [21].

In the very same year, an ethnopharmacological field survey was also conducted in the municipality of Tlanchinol Hidalgo, Mexico in which it was further confirmed that *O. rosea* has the potential to cure inflammations [24]. In addition to the methanolic extract, aqueous extract of *O. rosea* also possesses strong anti-inflammatory activity. This activity can be attributed to several secondary metabolites present in *O. rosea* with no toxic effects at the administrated doses [25].

*O. laciniata* was also claimed to possess important pharmacological activities. The dichloromethane fraction of *O. laciniata* extract was used to evaluate the anti-inflammatory activity. The extract effectively inhibited lipopolysaccharide-induced NO, PGE(2), and proinflammatory cytokine production in RAW264.7 cells [26].

Multiple sclerosis is the most chronic inflammatory disorder. In year 2009, a study was conducted to assess the potential therapeutic effects of *O. biennis* L. on multiple sclerosis patients. It was found that evening primrose oil intake has prevented multiple sclerosis and several other inflammatory diseases [27]. The polyphenolic extract of *O. paradoxa* was also found to have a potent anti-inflammatory action in the gastrointestinal tract [28]. A year later, *O. biennis* was found to be effective in the treatment of ulcerative colitis, Crohn's disease and also inflammatory bowel disease [29]. In year 2010, anti-inflammatory activity of defatted seeds extract of *O. paradoxa* was assessed. In this study, *ex vivo* effect of an aqueous extract of *O. paradoxa* on the formation of neutrophil-derived oxidants

was analyzed. The lipophilic extract constituents such as ellagic acid, gallic acid, (+)-catechin, and penta-*O*-galloyl- $\beta$ -D-glucose and a hydrophilic fraction containing polymeric procyanidins were also tested. The extract exhibited effective antioxidant effects against both formyl-met-leu-phenylalanine-induced and 4 $\beta$ -phorbol-12 $\beta$ -myristate- $\alpha$ 13-acetate-reactive oxygen species production in neutrophils with IC<sub>50</sub> values around 0.2  $\mu$ g/mL the antioxidant activity was attributed to all types of polyphenolics with penta-*O*-galloyl- $\beta$ -D-glucose being most potent constituent of the extract [30].

Evening primrose oil extracted by cold-pressed from *O. biennis* L. seeds is a vital source of appealing minor compounds, like tocopherols, long-chain fatty alcohols and sterols. It was reported that the sterols present in the oil may have a protective effect on some mediators involved in inflammatory damage development, signifying its potential value as a putative functional component of evening primrose oil [31].

The aerial parts of *O. paradoxa* and *O. biennis* were investigated for their anti-inflammatory activity in 2013. It was found that both the extracts exhibited anti-inflammatory activity by the inhibition of hyaluronidase and lipoxygenase in a concentration-dependent manner. The stronger activity of *O. biennis* extract toward lipoxygenase was attributed to its higher oenothien B content [32].

#### 2.4. Anti-cancer and anti-tumor activity

The prevention and treatment of cancer using herbal medicines has gained increased interest from the past few years. In 1999, it was reported for the first time that evening primrose oil may be of value in nutritional approaches of mammary gland tumor therapies [29]. Few years later, an experiment was conducted on female mice that were injected s.c. with  $5 \times 10^6$  Sp6 syngeneic cells that lead to the formation of solid tumor in them within 7–10 days. Tumor volume was monitored daily. They were then given an evening primrose oil enriched diet. It was then observed that the defatted seeds of *O. biennis* have anti-tumor potential and its activity appears selective for bone marrow-derived tumor cells [33].

A study was carried out in 2010 to compare the anticancer activity of defatted seed extract of *O. paradoxa* Hudziok (EPE) with the activity of individual constituents of the extract: (+)-catechin, pentagalloylglucose, gallic acid and the procyanidin fraction, as well as an evaluation of the combined effect of EPE and vincristine in the absence or presence of MRP1 (indomethacin) and P-glycoprotein (verapamil) inhibitors, on two human cancer cell lines, hepatoma (HepG2) and metastatic melanoma (HTB-140). The collective use of EPE (25  $\mu$ g/mL) and vincristine (1  $\mu$ M) in HTB-140 and HepG2 cells produced an increased cytotoxicity as compared to vincristine alone by more than 4 and 1.5 times, respectively. It was also found that EPE, containing pentagalloylglucose and procyanidins, appreciably increased the sensitivity of cancer cells, predominantly the melanoma cells, to the action of vincristine [33].

In year 2011, *O. paradoxa* was found to possess anti-migratory, anti-invasive and anti-metastatic potential towards prostate and breast cancer cells [34].

It was found in year 2014 that the polyphenols extract from *O. paradoxa* dose-dependently inhibits the growth of cancerous cells i.e., IEC-6, HT-29 and Caco-2 cells with Caco-2 being the most sensitive to the treatment [35].

The flavanol preparation of *O. paradoxa* was investigated to assess its influence on proliferation and invasiveness of human

prostate cancer cells (DU 145) and immortalized prostate epithelial cells. It was reported for the first time that the flavanol preparation of *O. paradoxa* reduces DU 145 cell proliferation (IC<sub>50</sub> = 97  $\mu$ M GAE for 72 h incubation) and invasiveness (by 24% versus control at 75  $\mu$ M GAE). It strongly inhibited immortalized prostate epithelial cells invasiveness in a concentration-dependent manner [36].

In an experiment conducted on the inhibition of MDA-MB-231 breast cancer cell viability and invasiveness by flavanol preparation of *O. paradoxa* defatted seeds, it was reported for the first time that the extract inhibits cell viability by increasing apoptosis and decreases cell invasiveness by decreasing angiogenesis [37].

In year 2017, a research was conducted on the roots of *O. biennis* to investigate its antiproliferative activity using MTT assay and by targeting ornithine decarboxylase and cathepsin D. It was founded that oenotheralanosterol B present in the roots exhibited strong antiproliferative activity against prostate, breast, hepatic and leukemia cancer cell lines as well as in mouse macrophages [IC<sub>50</sub> (8.35–49.69)  $\mu$ g/mL] as compared to the mixture of oenotheralanosterol A and oenotheralanosterol B [38].

#### 2.5. Treatment against kidney disorders

In 2009, an ethnobotanical survey of medicinal plants used in Loja and Zamora-Chinchi, Ecuador was conducted to explore their biological activities. It was reported after getting views from different people that aqueous extracts of fresh leaves of *O. rosea* and *Oenothera* sp. L (Onagraceae) have the potential to cure kidney disorders [10].

#### 2.6. Nematicidal activity

Plant-parasitic nematodes have been one of the most notorious plant pathogens worldwide. In year 2001, the nematicidal activity of aqueous extract of *Oenothera affinis* was tested against *Xiphinema americanum*. The study showed that the plant extract causes nematode immobility after 24 h [39].

#### 2.7. Immune response activity

Herbal medicines are in great demand in the developed world as they offer therapeutics for age-related disorders like memory loss, immune disorders, etc. with no side effects. In 2014, it was reported that the ethanolic extract of *O. paradoxa* exhibits dual stimulus-dependent effect on the respiratory burst in human leukocytes [40].

#### 2.8. Anti-bacterial activity

Bacterial infections are responsible for many deaths each year. Therefore, there is an urgent need to replenish our arsenal of anti-infective agents. The plant-derived compounds having antibacterial properties are attracting increasing attention. In 2009, it was that the methanolic extract of seeds of *O. biennis* L. showed strong antibacterial activity against four microorganisms i.e., *Candida albicans*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Escherichia coli* [9]. Few years later, it was found that antibacterial effect of methanolic and aqueous extracts *O. rosea* were also of benefit as an adjuvant treatment of diseases caused by the enterobacteria [41].

### 2.9. Anti-neuropathic activity

It is noted fact that, the breast cancer survivors who receive adjuvant chemotherapy sometimes may suffer from the late effects of chemotherapy including neuropathy, osteoporosis, congestive heart failure and premature menopause. A research carried out in 2003 showed that *O. biennis* plays a very important role for the patients suffering from chemotherapy-induced neuropathy. The patients taking *O. biennis* rich in  $\gamma$ -linolenic acid and linoleic acids exhibited improvements in nerve function measurements and symptoms [42].

### 2.10. Hypocholesterolemic activity

In the late 90s, a comparative study of hypocholesterolemic effects of six dietetic oils in cholesterol-fed rats was carried out. The results of this study demonstrated that *O. biennis* Linn oil inhibits the increasing serum total cholesterol and very low density lipoprotein, intermediate density lipoproteins and low density lipoprotein cholesterol concentrations in the presence of surplus cholesterol in the diet after long-term feeding [43,44].

### 2.11. Thrombolytic activity

Medicinal plants have many therapeutic agents that have antithrombotic, antibacterial *etc* activities. In year 1998, it was reported that the dietary supplementation with *O. biennis* enhances the antithrombotic ability of the endothelium, reduced sub-endothelial thrombogenicity and lessen the extent of vascular wall lesions caused by the hyperlipemic diet [45].

### 2.12. Cariostatic activity

Dental caries continue to be one of the most common oral health problems. Herbal products are used traditionally for the treatment of oral diseases. In an experiment, the inhibitory effects of *O. biennis* seed extract on the development of dental caries caused by *Streptococcus mutans* in rats were determined. It was then proclaimed that *O. biennis* seed extract has strong caries-inhibitory effects [46].

### 2.13. Anti-ulcerogenic effects

There are many products available for the treatment of gastric ulcers. Plant extracts are some of the most remarkable sources of new drugs, and have been shown to produce promising results for the management of gastric ulcers. A study was conducted on rats to find the anti-ulcerative effects of evening primrose oil. It was reported that *O. biennis* had shown significant anti-ulcer and cytoprotective effect on various experimentally induced gastric lesions [47].

### 2.14. Anthelmintic activity

Medicinal plants are a rich source of botanical anthelmintics and are used extensively for the treatment of many parasitic infections. The anthelmintic activity in genus *Oenothera* was reported for the first time in 2012 in *O. rosea*. Research showed that the aqueous and ethanolic extract of roots and stems displayed anthelmintic activity in a dose dependant manner. It was

also found that the ethanolic extract of stems exhibited most significant anthelmintic activity as compared to the ethanolic extracts of roots and also the ethanolic extracts of both stems and roots were more effectual than their aqueous extracts [2].

### 2.15. Curing hepatic disorders

In an ethanobotanical survey, it was found that the aqueous extract of whole fresh plant of *Oenothera pubescens* Willd and aqueous extract of fresh leaves of *O. rosea* have the potential to cure hepatic pains [10,18].

### 2.16. Anti-fungal activity

Novel antifungals are in high demand as there is a growing resistance to antifungal substances currently in use. In a research carried out in 1999, it was found that the roots of *O. biennis* are involved in anti-fungal activity against *Fusarium semitectum*, *Fusarium fusiformis* and *Alternaria alternate* showing highest activity against *Fusarium semitectum* [48].

### 2.17. Anti-diarrheic activity

A preliminary study on the antidiarrhoeic activity of different Mexican plants including *O. rosea* was conducted. The test was performed on diarrheic mice and it was reported that *O. rosea* showed quite significant diarrheal inhibition than other plant species used for the study [49].

### 2.18. Antiviral activity

In the present era, the demand of new compounds having antiviral properties has increased a lot as the available antiviral drugs have proven to be unsatisfactory for treating viral infection. This is due to the viral resistance of recurrent viral infections in immunocomprised patients. Medicinal plants with significant pharmacological activities are now being used for this purpose. In year 1995, a United State copyright was granted to an antiviral composition comprising an aqueous extract of *Oenothera caespitose*. The composition of such an extract is especially efficient in treating contemporary herpes simplex lesions and also endorses healing of lesions caused by the herpes simplex virus, Epstein–Barr virus and varicella virus. The composition may also reduce the reappearance of herpes simplex lesions and act as a prophylactic agent by interrupting the spreading of the virus and subsequent vesicle and lesion formation [50,51].

### 2.19. Treatment of cardiac disorders

In year 2012, a study was conducted to evaluate the *in vitro* reactive oxygen species generation and inhibition of neutral endopeptidase activity by an aqueous extract of *O. paradoxa* in neutrophils obtained from healthy volunteers and from patients after acute myocardial infarction. It was concluded that a dose of *O. paradoxa* extract at concentrations of 20, 50 and 100  $\mu\text{g}/\text{mL}$  resulted in a considerable decline in neutral endopeptidase activity in both groups. Therefore, it was suggested that, this extract appears to be an attractive candidate for supplementation in the deterrence of cardiovascular diseases [52].

**Table 1**Compounds isolated and identified from genus *Oenothera*.

Plant species	Plant parts investigated	Isolated compounds	Refs
<i>Oenothera albicaulis</i>	Flowers	Alkaloids: oxindole-3-acetic acid methyl ester, phenethylamine Esters: methyl benzoate, methyl anthranilate Carboxylic acids: phenylacetic acid Alcohols: benzyl alcohol	[55]
<i>O. biennis</i>	Roots	Esters: methyl and ethyl esters of gallic acid, methyl ester of protocatechuic acid Alcohols: 2-methyl-7-oxo-tritetracont-1,5-dien-21-ol, 5-methyl-27-oxo-triacont-4-en-24-ol Triterpenoids: oleanolic acid, maslinic acid Fatty acids: 18-hydroxypentacos-21-en-1-oic acid, betulinic acid, morolic acid oleic acid, $\gamma$ -linolenic acid, linoleic acid Phenolic acids: salicylic acid, gentisic acid, vanillic acid, caffeic acid, p-hydroxybenzoic acid, protocatechuic acid, p-coumaric acid, ferulic acid, p-hydroxyphenylacetic acid, syringic acid, gallic acid, 2-hydroxy-4-methoxybenzoic acid, 2,7,8-trimethyllellagic acid, tetramethyllellagic acid Lactones: oenotheraphenoxylactone, oenotheraphytyllactone Flavonoids: catechin, epicatechin, isoflavones, chalcones	[56] [57] [7,14] [48,56-58] [56-63]
	Seeds	Esters: methyl and ethyl esters of gallic acid, methyl ester of protocatechuic acid Alcohols: 2-methyl-7-oxo-tritetracont-1,5-dien-21-ol, 5-methyl-27-oxo-triacont-4-en-24-ol Triterpenoids: oleanolic acid, maslinic acid, betulinic acid, morolic acid Fatty acids: 18-hydroxypentacos-21-en-1-oic acid, oleic acid, $\gamma$ -linolenic acid, linoleic acid Phenolic acids: salicylic acid, gentisic acid, vanillic acid, caffeic acid, p-hydroxybenzoic acid, protocatechuic acid, p-coumaric acid, ferulic acid, p-hydroxyphenylacetic acid, syringic acid, gallic acid, 2-hydroxy-4-methoxybenzoic acid, 2,7,8-trimethyllellagic acid, tetramethyllellagic acid Lactones: oenotheraphenoxylactone, oenotheraphytyllactone Flavonoids: catechin, epicatechin, isoflavones, chalcones Tannins: penta-O-galloyl- $\beta$ -D-glucose, dimeric ellagitannins OeB, trimeric ellagitannins OeA, tetrameric ellagitannins, pentameric ellagitannins, hexameric ellagitannins and heptameric ellagitannins Triterpenoids: lupeol, 7,24-tirucalladienol, cycloartenol, 24-methylene cycloartenol, oenotheralanosterol A, oenotheralanosterol B Sterols: phytosterol: $\beta$ -sitosterol, campesterol, germanicol Fatty alcohols: hexacosanol, tetracosanol, docosanol, octacosanol Chalcone: 2-hydroxychalcone	[15] [56,60]
<i>O. paradoxa</i>	Seeds	Esters: ethyl gallate, catechin gallate, (-)-epicatechin gallate Phenolic acids: gallic acid, ellagic acid Flavonoids: quercetin-3-O-glucoside, quercetin-3-O-glucuronide, quercetin-3-O-pentoside	[64,65]
<i>O. speciosa</i>	Leaves and stem	Tannins: penta-O-galloyl- $\beta$ -D-glucose, Oenothetin B, proanthocyanidin B3 Esters: methyl esters of caffeic acid, chlorogenic acid and gallic acid Flavonoids: quercetin, myricetin, myricetin-4'-O- $\alpha$ -L-rhamnopyranoside, quercetin 3'-O- $\alpha$ -L-rhamnopyranoside, hyperin, europetin 3-O- $\alpha$ -L-rhamnopyranoside, rhamnetin 3-O- $\beta$ -galactopyranoside Biflavonols: speciin	[26,66] [9]
<i>Oenothera lamarckiana</i>	Seeds	Phenolic acids: salicylic acid, gentisic acid, p-hydroxybenzoic acid, vanillic acid, protocatechuic acid, p-coumaric acid, caffeic acid, ferulic acid, p-hydroxyphenylacetic acid, syringic acid, gallic acid, 2-hydroxy-4-methoxybenzoic acid Tripenoidal Esters: 3-O-trans-caffeoyl derivatives of betulinic acid, morolic acid and oleanolic acid	[26,61]
<i>O. laciniata</i>	Roots and stems	Triterpenoid: asiatic acid Flavonoid: quercetin Tannins: oenothetin A and B, oenothetin C, oenothetin D, oenothetin F and oenothetin G6-tri-O-galloyl- $\beta$ -D-glucose, cornusiin B, tellimagrandin I, eucalbanin B	[67,68]
<i>Oenothera hoelscheri</i>	Aerial parts	Esters: valoneic acid dilactone methyl ester (XIX) Flavonoids: kaempferol-3-O- $\beta$ -glucuronide, quercetin-3-O- $\beta$ -glucuronide, kaempferol-3-O-(2''-O-galloyl)- $\beta$ -glucuronide, quercetin-3-O-(2''-O-galloyl)- $\beta$ -glucuronide, myricetin-3-O- $\beta$ -glucuronide, kaempferol-3-O-rhamnopyranoside, quercetin-3-O- $\beta$ -galactoside, kaempferol-3-O- $\beta$ -glucoside, kaempferol-3-O- $\beta$ -glucuronide methyl ester, quercetin-3-O- $\beta$ -glucuronide methyl ester, quercetin-3-O- $\beta$ -glucoside	[69]
<i>Oenothera cheiranthifolia</i>	Whole plant	Triterpenoids: cheiranthic acid, asiatic acid oleanane, ursane Flavonoids: quercetin-3-O-glucuronide, myricetin-3-O-glucuronide	[70]

Table 1 (continued)

Plant species	Plant parts investigated	Isolated compounds	Refs
<i>Oenothera odorata</i>	Seeds	Flavonoids: quercetin, 3-O-methylquercetin, quercetin-3-O-galactoside, quercetin-3-O-rhamnoside, quercetin-3-O-glucuronide, quercetin-3-O-methylglucuronide Anthocyanins: cyanidin-3-O-glucoside, 5-O-diglucoside	[71]
<i>O. rosea</i>	Whole plant Stems and leaves	Flavonoids: quercetin, quercetin 3-O-β-D-allopyranoside-3'', 6''-diacetate 6-Hydroxygenistein-7-O-(rhamnosyl-[1 → 2]-4-acetylramnoside), Quercetin-3-O-(2-galloylglucoside), Quercetin-3-O-{glucosyl-[1 → 2]-xylosyl-[1 → 6]-glucoside} (XX), Quercetin-3-O-{glucosyl-[1 → 6]-glucosyl-[1 → 2]-rhamnoside}, Quercetin-3-O-{6-benzoylglucosyl-[1 → 4]-xyloside}, Luteolin-4-O-{rhamnosyl-[1 → 2]-glucosyl-[1 → 4]-2-acetylramnoside}, Luteolin-4-O-{glucosyl-[1 → 6]-glucoside}, Apigenin-4-O-{4-acetylramnose-[1 → 2]-2-acetylglucose}, Morin-7-O-{2,6-diacetylglucoside}, Quercetin-3-O-{6-malonylglucoside} Phenolic acid: gallic acid Triterpenoid: ursolic acid Esters: methyl hexadecanoate, ethyl-6-methylpentadecanoate, methyl-3-tert-butyltetradec-5-en-11-ynoate, methyl-3, 11,14-trimethylheptadecanoate Alkaloids, Quinones, Tocopherol, Lactones, Tannins, Saponins (only screening)	[3,72–74]
<i>Oenothera tetraptera</i>	Leaves	Tannins: Oenotherin T1, 1,6-di-O-galloyl-β-D-glucose, 1,2,3-tri-O-galloyl-β-D-glucose, 1,2,6-tri-O-galloyl-β-D-glucose	[72]
<i>Oenothera gigas</i>	Aerial parts	Phenolic acids: protocatechuic acid and p-hydroxybenzoic acid Flavonoids: quercetin-3-O-rhamnoside, quercetin-3-O-galactoside	[75]
<i>Oenothera berteriana</i>	Seeds	Flavonoids: quercetin, 3-O-methylquercetin, quercetin-3-O-galactoside, quercetin-3-O-rhamnoside, quercetin-3-O-glucuronide Anthocyanins: cyanidin-3-O-glucoside, 5-O-diglucoside	[70]
<i>Oenothera hookeri</i>	Leaves	Flavonoids: quercetin-7-O-rhamnoside, quercetin-3-O-glucoside, (hyperoside), quercetin-3-arabinoside, kaempferol galactoside, rutin	[73]
<i>Oenothera brachycarpa</i>	Leaves	Flavonoids: vitexin, isovitexin, orientin, luteolin-7-O-rutinoside	[76]
<i>Oenothera maritima</i>	Aerial parts	Triterpenoids: 2α, 3α, 20β, 23-tetrahydroxy-ursa-12,19(29)-dien-28-oic acid, 2α, 3α, 20β, 23-tetrahydroxy-ursa-12,19(29)-dien-28, 20β – lactone, 2α, 3α-dihydroxy-ursa-12,19-dien-28-oic acid 28-O-β-D-glucopyranoside, 2α, 3α, 23-trihydroxy-ursa-12,19(29)-dien-28-oic acid, 2α, 3α, 23-trihydroxy-ursa-12,19(29)-dien-28-oic acid 28-O-β-D-glucopyranoside, 2α, 3α, 23-trihydroxy-ursa-12,18-dien-28-oic acid, 2α, 3α, 23-trihydroxy-ursa-12,18-dien-28-oic acid 28-O-β-D-glucopyranoside, 2α, 3α, 19α-trihydroxy-24-norursa-4(23), 12-dien-28-oic acid, myriantiacid and arjunolic acid	[77]

## 2.20. Vasorelaxation activity

Aging deteriorates vascular functions such as vascular reactivity and stiffness. There are various reports that suggest that bioactive compounds can improve vascular functions. An experiment was conducted on rats to determine the effect of ethanol extract of *Oenothera odorata* on vascular relaxant activity. For this, the rats were sacrificed by cervical dislocation. The carotid artery from rats was carefully dissected from surrounding fat and connective tissues and was immediately placed in ice-cold Krebs–Ringer solution (118 mM NaCl, 4.7 mM KCl, 1.1 mM MgCl<sub>2</sub>, 1.2 mM KH<sub>2</sub>PO<sub>4</sub>, 1.5 mM CaCl<sub>2</sub>, 25 mM NaHCO<sub>3</sub>, and 10 mM glucose, pH 7.4) and aerated with 95% O<sub>2</sub>–5% CO<sub>2</sub>. The effects of K<sup>+</sup> channel inhibitors on the *O. odorata* induced vasorelaxation were tested. It was found that activation of K<sup>+</sup> channels, K<sup>+</sup> ATP channels in particular, is involved in the ESOO-induced vasorelaxation [53].

## 3. Phytoconstituents

A very large number of diverse phytoconstituents have been reported in genus *Oenothera*. These phytoconstituents included some esters, alkaloids, fatty acids, fatty alcohols, phenolic acids, flavonoids, tannins, triterpenoids, quinones, tocopherol,

saponins, lactones, sterols and biflavonols [54] which are listed in Table 1.

## 4. Conclusions

The plant of genus *Oenothera* have emerged as a good source of medicines for the treatment of diarrhea, neurogenerative disorders, kidney problems and immune disorders. The crude extracts of these plants have also exhibited a wide range of *in vitro* and *in vivo* pharmacological effects, including anti-inflammatory, anti-oxidant and anti-microbial.

A large number of phytoconstituents have been isolated and identified from different parts of different species of *Oenothera*. Flavonoids, phenolic acids and triterpenoids are most commonly found in these species. Other constituents include esters, alkaloids, sterols, saponins, alcohols *etc.* Valoneic acid dilactone methyl ester is a unique compound found in this genus. It has only been identified in *Oenothera hoelscheri*. The most investigated species was *O. biennis* in terms of phytoconstituents and pharmacological studies. There are other species too that hold great pharmacological importance. This review article provides an insight to the researchers regarding further exploration of unexplored species of this genus so that they can also be used as herbal drugs to cure various ailments.

## Conflict of interest statement

The authors declare that they have no conflict of interest.

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