Received: 31 May 2019 | Revised: 28 September 2019 | Accepted: 10 October 2019
DOI: 10.1002/ptr.6540

REVIEW

WILEY

Convolvulus plant—A comprehensive review from phytochemical composition to pharmacy

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Convolvulus genus is a representative of the family of Convolvulaceae. *Convolvulus* plants are broadly distributed all over the world and has been used for many centuries as herbal medicine. *Convolvulus* genus contains various phytochemicals such as flavonoids, alkaloids, carbohydrates, phenolic compounds, mucilage, unsaturated sterols or terpenes, resin, tannins, lactones, and proteins. This review highlights the

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Funding information
CONICYT PIA/APOYO CCTE, Grant/Award Number: AFB170007

phytochemical composition, antimicrobial and antioxidant activities, application as food preservative, traditional medicine use, anticancer activities, and clinical effectiveness in human of *Convolvulus* plants. All the parts of *Convolvulus* plants possess therapeutic benefits; preliminary pharmacological data validated their use in traditional medicine. However, further preclinical and clinical experiments are warranted before any application in human health.

KEYWORDS

anticancer, antimicrobial, antioxidant, *Convolvulus*, food preservative, pharmacological properties, traditional uses

1 | INTRODUCTION

Plants are considered a valuable source of natural compounds that exhibit different biological and pharmacological activities (Abdolshahi et al., 2018; Mishra et al., 2018; Mishra et al., 2018; Salehi et al., 2018). Since centuries, many different plants and their phytoconstituents have been used in both traditional and modern medicine purposes in the world (Prakash et al., 2018; Salehi et al., 2018; Sharifi-Rad et al., 2018). Convolvulaceae (the morning glory family) is a family of plants from the order of Solanales covering over 1,880 species in 57 types. They are found on all continents except for circumpolar areas (Staples, 2006; Staples & Austin, 2009; Staples & Noltie, 2007). *Convolvulus* (convolere) is a genus of the Convolvulaceae family (bindweed or glory family), which is one of the medicinally and economically important family, including about 250 species of flowering plants, present as trees, shrubs, and herbs (Al-Snafi, 2015; Chen, Lu, Yang, Li, & Fan, 2018; Nacef, Jannet, Abreu, & Mighri, 2010; Staples, 2006; Staples & Austin, 2009; Staples & Noltie, 2007). The use of the Latin and common name of *Convolvulus* plants for each species was complicated before the currently accepted names because of the widespread of this family in the world (Al-Snafi, 2015; Austin, 2008). The greatest diversity of *Convolvulus* plants has been found in Western and Central Asia, Mediterranean, Macaronesia, East Africa, and Arabia (Carine, Alexander, & Russell, 2003; Ranjbar, Ezazi, & Ghahremaninejad, 2017). Some common species of this genus include *Convolvulus lineatus* L. (Berjano et al., 2013; Gapparov, Razzakov, Abdullabekov, & Aripova, 2008), *Convolvulus prostratus* Forssk. (Bihaqi, Sharma, Singh, & Tiwari, 2009; Kizhakke, Olakkaran, Antony, Tilagul, & Hunasanahally, 2019), *Convolvulus althaeoides* L. (Cabrita, 2015; Tawaha, Alali, Gharaibeh, Mohammad, & El-Elimat, 2007), *Convolvulus arvensis* L. (Al-Enazi, 2018), and *Convolvulus pilosellifolius* Desr. (Al-Enazi, 2018; Al-Rifai et al., 2017; Awaad et al., 2016).

Researchers have paid attention to *Convolvulus* plants and their corresponding extracts and oils because of their important phytochemical composition, bioavailability, clinical effectiveness, and safety (Chen et al., 2018). Recently, extensive studies conducted on the biological activities of *Convolvulus* species such as antioxidant effects of the *C. prostratus* (Singh & Vora, 2017) and *C. pilosellifolius* (Al-Rifai et al., 2017). Plants belonging to *Convolvulus* genus contain various complex chemical profiles including flavonoids, steroids, terpenoids, carbohydrate, amino acids, anthraquinones (Al-Rifai et al., 2017), anthocyanidins, phenylpropanoids, coumarins, lignans, resins (Chen et al., 2018), tannins, saponins (Manbir & Kalia, 2012), alkaloids, lipids (Manbir & Kalia, 2012), essential oils (Dehghan, Sarrafi, & Salehi, 2015), and caffeoylquinic acid derivatives (El-askary, Abou-hussein, Shehab, & Sleem, 2006).

Naturally occurring chemicals from *Convolvulus* species are considered to be an organic food preservative for controlling the food spoilage. Antioxidant and antimicrobial activities of natural compounds prevent lipid oxidation and growth of food pathogens and extend their shelf life. *C. arvensis* ethanol extract has been applied on beef patties to prevent lipid oxidation (Azman, Gallego, Julia, Fajari, & Almajano, 2015).

Convolvulus plants have great medicinal value to humanity and society. The pharmacological potential of these plants comes from their chemical constituents with biological activities. Pharmacological activities were reported on some *Convolvulus* species such as the use of *C. pilosellifolius* as an antiulcerogenic (Atta, Mohamed, Nasr, & Mouneir, 2007; Awaad et al., 2016), *C. arvensis* and *C. pilosellifolius* inhibited tumor growth (Al-Enazi, 2018; Meng et al., 2002), and *C. prostratus* against Alzheimer's disease (Kizhakke et al., 2019) and treat stress-induced neurodegeneration (Rachitha et al., 2018), while *C. prostratus* for preventing aluminum-induced neurotoxicity (Bihaqi et al., 2009). Indeed, the significance of *Convolvulus* plants is not only for medicinal applications but also for ancient and religious significance because it reminded people of certain aspects of their gods and goddesses (Austin, 2008). *Convolvulus* plants include a large number of important species, which have the properties of treatment of serious diseases such as fever, loss of memory, insomnia, heart disease, and hair growth (Sethiya & Mishra, 2010). A number of reviews were published on some specific activities of *Convolvulus* plants (Al-Snafi, 2015; Austin, 2008; Chen et al., 2018). This comprehensive review covers the characteristics, phytochemical composition, antimicrobial and antioxidant activities, application as food preservative, traditional medicine use, anticancer activities, and clinical effectiveness in human of *Convolvulus* plants.

2 | CHARACTERISTICS OF *CONVOLVULUS* PLANTS

The *Convolvulus* genus has 75 plants as listed in The Plant List (theplantlist.org). The Plant List (2019). Version 1.1. Published on the Internet; http://www.theplantlist.org/ (accessed 1st February). Most species are winding or upright herbaceous plants, with several winding shoots, as well as trees and shrubs. Stems often contain latex. Shoots are usually herbaceous, although many of them become woody with age. The shape of the stem varies from cylindrical to 1- or 3-flap and is often asymmetrical or flat. Part of the variability of the family of bipinnatus stems from the creation of cambium, which produces concentric xylem rings with attached phloem bands (Austin, 1971).

The leaves are spiral, straight, and whole to layered. Leaf blades are usually straight-hearted. Most lianas have such leaf blades that differ in shape: ovate and oblong to lanceolate, their bases are mostly blunt to sharp (Acevedo, 2017; Austin, McDonald, & Murguía-Sánchez, 2012; Simão-Bianchini, Ferreira, & Pastore, 2014; Staples, 2006). The flowers are actinomorphic, effective, and almost always bisexual, five-fold. They grow in the tips and in leaf angles; they can also be clustered; and sometimes they appear singly (Calystegia) or in clusters. Seeds are smooth or hairy; the embryo is large with broad-folded or bent cotyledons. Seeds are large, four per capsule. Species with hard coat covers have a shelf life of at least 30 years; in turn, those from tropical taxa that do not have hard seeds live for a short time, a week or two. Many species have hard, cartilaginous endosperm; others do not have this and have distinctive peripheries (Preston, 2013). Tubers are of root origin, usually fibrous-form root or tuber shoots (Preston, 2013; Ravi, Naskar, Makeshkumar, Babu, & Krishnan, 2009).

3 | *CONVOLVULUS* PLANTS PHYTOCHEMICAL COMPOSITION

The major components of *Convolvulus* species are shown in Table 1 and Figure 1 (chemical structures).

3.1 | *Convolvulus althaeoides* L.

Gas chromatography and gas chromatography–mass spectrometry analyses of *C. althaeoides* flowers essential oil reveal the presence of 95% of sesquiterpene hydrocarbons, oxygenated sesquiterpenes, and oxygenated monoterpenes classes viz. *trans*-pinocarveol, verbenone, *trans*-verbenol, *trans*-carveol, β-maaliene, methyl carvacrol, α-copaene, 2,5-dimethoxy-*p*-cymene, β-caryophyllene, α-humulene, germacrene D, (*E*)-geranylacetone, β-selinene, (*E*,*E*)-α-farnesene, *cis*-β-guaiene, germacrene B, δ-cadinene, *cis*-arteannuic alcohol, caryophyllene oxide, 1-epi-cubenol, τ-muurolol, τ-cadinol, α-cadinol, and pentadecanal (Hassine et al., 2014). Also, an acylated anthocyanin trioside was isolated from pink flowers of *C. althaeoides* using a combination of chromatographic technique, cyanidin 3-*O*-[6-*O*-(4-*O*-(6-*O*-(*E*-caffeoyl)-β-D-glucopyranosyl)-β-L-rhamnopyranosyl)-β-D-glucopyranoside]-5-*O*-β-D-glucopyranoside (Cabrita, 2015).

3.2 | *Convolvulus arvensis* L.

Many authors studied the phytochemical constitution of *C. arvensis* and showed that it mainly consists of carbohydrates, coumarins, saponins, flavonoids, lipids, steroids or terpenoids, sugar derivatives of

TABLE 1 Major components of *Convolvulus* spp

Plant species	Major components	Reference
Convolvulus althaeoides L.	Sesquiterpene hydrocarbons, oxygenated sesquiterpenes, and oxygenated monoterpenes: germacrene D, τ-cadinol, and verbenone	(Hassine et al., 2014)
Convolvulus arvensis L.	Sterols, triterpenes, flavonoids, tannins, alkaloids, saponins, phlorotannins, cardiac glycosides, coumarins	(Al-Enazi, 2018; Bazzaz & Haririzadeh, 2003; Borchardt et al., 2008; Edrah, Osela, & Kumar, 2013; Khan, Ghori, & Hayat, 2015; Miri, Sharifi Rad, Mahsan Hoseini Alfatemi, & Sharifi Rad, 2013; Raza et al., 2012; Ullah, Sohail, Niaz, Khan, & Khattak, 2018)
Convolvulus lineatus L.	Flavonoid sulphates and flavones C and C-/O glycosides: apigenin, chrysin, genistein, hesperidin, isorhamnetin, kaempferol, luteolin, myricetin, naringenin, quercetin, rhamnetin, rutin, tricine, and vitexin	(Noori, Bahrami, Mousavi, Khalighi, & Jafari, 2017)
Convolvulus pilosellifolius Desr.	Sterols, triterpenes, flavonoids, tannins, alkaloids. Phellandrene, *p*-hydroxyphenyl-acetic acid, scopoletin, ferulic acid, syringic acid, pinosylvin, apigenin or galangin, naringenin, kaempferol or luteolin or fisetin, eriodictyol or aromadendrin, quercetin, taxifolin, scopolin, *protocatechuic acid or gentisic acid, vanillic acid, myricetin*	(Al-Enazi, 2018; Al-Rifai et al., 2017)
Convolvulus prostratus Forssk	Alkaloids, glycosides, flavonoids, steroids, and saponins	(Singh, Rathod, & Saxena, 2011; Verma et al., 2012)

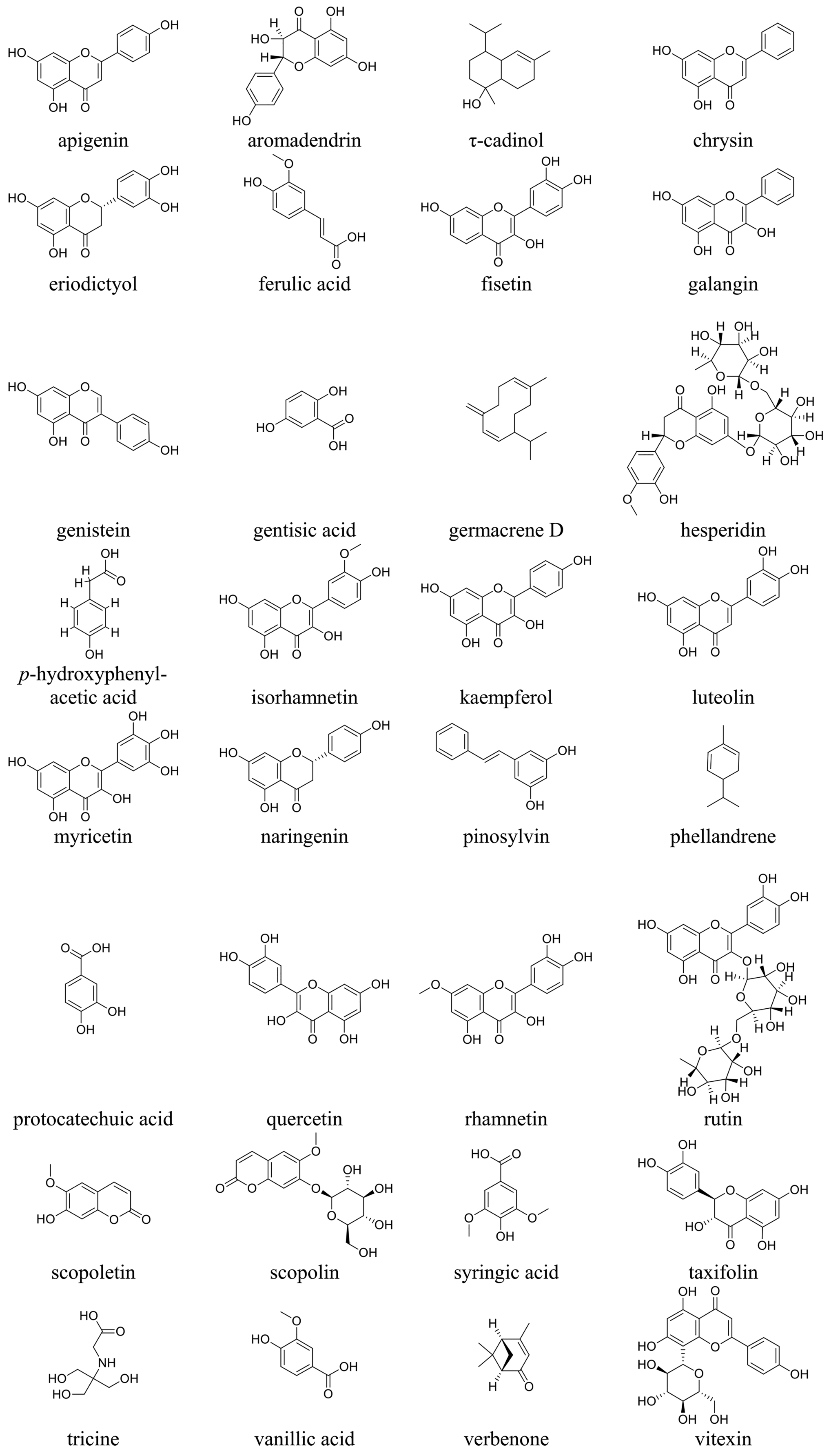

FIGURE 1 Chemical structures of major components of *Convulvulus* spp

kaempferol and quercetin, tannins, alkaloids, lactones, proteins or amino acids, arvensic acids A-D, and vitamin E (Al-Enazi, 2018; Ali et al., 2013; Armah-Agyeman, Gyamerah, Biney, & Woldesenbet, 2016; Atta & Mouneir, 2004; Awaad, Mohamed, El-Sayed, Soliman, & Mabry, 2006; Balah, 2016; Dhole, Dhole, Lone, & Bodke, 2012; Evans & Somanabandhu, 1974; Fan et al., 2018; Manbir & Kalia, 2012).

The coumarins present in *C. arvensis* are 7-hydroxycoumarin (umbelliferone), 6,7-hydroxycoumarin (esculetin), 6-methoxy-7-hydroxycoumarin (scopoletin), and 6-methoxycoumarin 7-*O*-glucoside (scopoletin 7-*O*-glucoside). The flavonoids detected in *C. arvensis* are 15-hydroxy isocostic acid, isocostic acid 4-carboxaldehyde, methyl 15-oxo-eudesome-4, 11(13)-diene-12-oate, 1α,9α-dihydroxyα-cyclocostunolide, isorhamnetin 3-sulphate, isorhamnetin 3-*O*-rutinoside, rhamnetin, epicatechin, 6,3′-dihydroxy-3, 5,7,4′-tetramethoxyflavone, 3,6,7,3′,4′-pentamethoxy flavone, 6,4′-dihydroxy-3, 7-dimethoxyflavone, 6,4-dihydroxy-3,5,7-trimethoxyflavone, protocatechic, *p*-hydroxybenzoic, syringic, vanillin, benzoic, ferulic, caffeic, gentisic, *p*-coumaric, syringic, vanillic, *p*-hydroxyphenylacetic, and *p*-hydroxybenzoic acids. The lipids present in *C. arvensis* are *n*-butyric, iso-butyric, palmitic, oleic, stearic, behenic, linolenic, linoleic, methyl-7,10-octadecadienoate, and arachidic acids.

The steroids or terpenoids detected in *C. arvensis* are α-amyrin, campesterol, stigmasterol, β-sitosterol, apigenin, chrysin, genistein, hesperidin, kaempferol, luteolin, myricetin, naringenin, quercetin, rutin, tricine, vitexin, cuscohygrine, dihydroquercetin, neophytadiene, hexadecanamide, 9-octadecanamide, 1,2-benzendicarboxylic acid, stigment-5-en-3-ol, 5-β-pregn-7-en-3,20-dione, quercetagetin 3,5,6,7,3′,4′-hexamethyl ether, sesquiterpene (eudesm-4(15),11(13)-diene-12,5β-olide), 3,5-dicaffeoyl quinic acid, β-methylesculetin, calystegins, convovulin, umbelliferone, chlorogenic acid, esculetin, scopoletin, and scopoletin-7-*O*-glucoside. The kaempferol sugar derivatives present in *C. arvensis* are 3-*O*-β-D-glucoside, 7-*O*-β-D-glucoside, 3-*O*-α-L-rhamnosyl, 7-*O*-β-D-glucoside, 3-*O*-rutinoside, 7-*O*-rutinoside, 3-*O*-α-L-rhamnoside, and 3-*O*-β-D-galactorhamnoside. The quercetin sugar derivatives are 3-*O*-α-L-rhamnoside and 3-*O*-rutinoside. The alkaloids present in *C. arvensis* are pseudotropine, tropine, tropinone, meso-cuscohygrine, hygrine, calystegines, and atropine.

3.3 | *Convolvulus lineatus* L.

The alcohol extract of *C. lineatus* flowers studied revealed the presence of glycosides, apigenin, chrysin, genistein, hesperidin, isorhamnetin, kaempferol, luteolin, myricetin, naringenin, quercetin, rhamnetin, rutin, tricine, and vitexin (Noori et al., 2017).

3.4 | *Convolvulus pilosellifolius* Desr.

C. pilosellifolius analysis revealed the major class of phytochemicals such as carbohydrates, glycosides, flavonoids, sterols, triterpenes, protein, amino acids, tannins, and alkaloids (Al-Enazi, 2018). Chromatographic and spectroscopic analyses identified compounds like kaempferol, quercetin, phellandrene, gentisic acid, vanillic acid, scopoletin, ferulic acid, *p*-hydroxyphenylacetic acid, syringic acid, protocatechuic acid, pinosylvin, apigenin, galangin, naringenin, luteolin, fisetin, eriodictyol, aromadendrin, taxifolin, myricetin, amanitate, and asmatol (Al-Rifai et al., 2017; Awaad et al., 2016).

3.5 | *Convolvulus prostratus* Forssk.

The qualitative analysis of *C. prostratus* reveals the presence of alkaloids, flavonoids, steroids, glycosides, fatty acids, terpenoids, tannins, proteins, amino acids, saponines, phenolic compounds, and resin (Balaji, Chek Hean, Ravichandran, & Sikarwar, 2014; Kaushik, Jain, & Majumder, 2017; Rachitha et al., 2018; Shalavadi, Chandrashekhar, & Muchchandi, 2018; Sharma, Bhatnagar, & Kulkarni, 2010; Sharma, Verma, & Prasad, 2014). Compounds, such as microphyllic acid, kaempferol, kaempferol-3-glucoside, 3,4 dihydroxycinnamic acid, scopoletin, convolamine, convolidine, sitosterols (Amin, Sharma, Vyas, Prajapati, & Dhiman, 2014; Garg et al., 2018; Kulkarni, Girish, & Kumar, 2012), 2-butanone, pentanoic acid, cinnamic acid, silane, decanoic acid, 2-pentanol, ascorbic acid, 10-bromodecanoic acid, tridecane, phthalic acid, eicosane, octatriacontyl pentafluoropropionate, 1-octadecanesulphonyl chloride, squalene, pyrimidine, heneicosane, 1,2-benzenedicarboxylic acid, cyclononasiloxane, octadecamethyl, nonacosane, sulphurous acid pentadecyl 2-propyl ester, straight chain hydrocarbons (C22–C33), fatty acids (C14–C28), fatty alcohols (C24–C32), vitamin E, and cyclononasiloxane, are found in this plant (Rachitha et al., 2018; Srivastava & Deshpande, 1975).

4 | ANTIMICROBIAL ACTIVITIES

Microbial infections are a worldwide threat to human as it is responsible for high morbidity and mortality. Although antibiotics have significantly contributed to their control, the uprising of dangerous and antibiotic-resistant pathogenic strains remain a major concern and underlined the need for new antibiotics. Natural products with chemical and structural diversities cannot be matched by any synthetic libraries of small molecules and remain the best sources of drug leads and drugs (Newman & Cragg, 2012). Besides the long-established clinical use, the plant-derived compounds display good tolerance and acceptance among patients and seem like a credible source of antimicrobials. Though there is a long history in the treatment of various diseases such as microbial infections using medicinal plants, and to date, only ~ 100,000 plant species have been explored (Schmidt et al., 2014) including *Convolvulus* plants.

4.1 | *Convolvulus pilosellifolius* Desr.

C. pilosellifolius is a commonly used medicinal plant that displayed bacteriostatic activity against *Bacillus subtilis*, *Pseudomonas aeruginosa*, and *Escherichia coli* with minimum inhibitory concentration (MIC) of 0.25, 1.06, and 0.93 mg/ml, respectively (Al-Rifai et al., 2017). In another study, Al-Enazi (2018) reported that 95% ethanol extract of aerial part of C. *pilosellifolius exhibited antibacterial activity against both Gram-negative (E. coli*, *Klebsiella pneumoniae*, *Proteus vulgaris*, *Ps. aeruginosa*, *Salmonella* Typhimurium*) and Gram-positive (B. subtilis*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus pyogenes) with MIC values of 0.004–31.25 mg/ml. The same extract also showed fungistatic activity against Aspergillus fumigatus*, *Candida albicans*, *Candida tropicalis*, *Geotrichum candidum*, *Microsporum canis*, and *Trichophyton mentagrophytes* with MIC values of 0.004–1.0 mg/ml (Al-Enazi, 2018; Table 2).

4.2 | *Convolvulus* arvensis L.

Different solvent extracts of leaves and stems of C. arvensis exhibited antibacterial activity against Staph. aureus, Staph. epidermidis, Staph. saprophyticus, B. subtilis, Acinetobacter junii, Acinetobacter baumannii, K. pneumoniae, Enterobacter aerogenes, Enterococcus faecalis, E. coli, Ps. aeruginosa, P. vulgaris, Shigella dysenteriae, Vibrio cholera, Proteus mirabilis, S. Typhimurium, Salmonella paratyphi, Serratia marcescens, S. pyogenes, and Enterobacter cloacae with butanol, chloroform, and acetone extracts that were the most potent (Al-Enazi, 2018; Bazzaz & Haririzadeh, 2003; Borchardt et al., 2008; Edrah et al., 2013; Khan et al., 2015; Miri et al., 2013; Raza et al., 2012; Ullah et al., 2018). *C.* arvensis likewise exhibited *antifungal activity against* A. fumigatus, C. albicans, C. tropicalis, G. candidum, M. canis, and T. mentagrophytes with MIC values of 0.001–0.156 mg/ml (Al-Enazi, 2018; Hassawi & Kharma, 2006; Table 2).

4.3 | *Convolvulus* prostratus Forssk.

Verma et al. (2012) reported the antibacterial activity of the methanolic extract of the whole plant of *C. prostratus* against *Staph. aureus* and *E. coli*. As well, *C. prostratus saponins produced* by both in vitro and in vivo techniques *from leaves showed* antibacterial activity against *E. coli*, *Staph. aureus*, and *B. subtilis* (Singh et al., 2011; Table 2).

5 | ANTIOXIDANT ACTIVITIES

Once formed, free radicals as highly reactive species may trigger oxidative chain reaction. Antioxidants play a role of the body defense system as they can safely interact with free radicals and terminate the chain reaction thereby preventing cellular damage, which leads to a variety of diseases (Fang, Yang, & Wu, 2002).

The literature indicated that *Convolvulus* plants possess antioxidant activity both in vitro and in vivo that likely depends on the species, the species organ (whole plant, aerial parts, flowers, or leaves), extraction solvent, and concentration (Table 3).

C. pilosellifolius showed 1,1-diphenyl-2-picrylhydrazyl (DPPH) scavenging properties with half-maximal inhibitory concentration (IC_{50}) 38.0 μg/ml and the inhibition rate of 90.2% (Al-Rifai et al., 2017). Methanolic extracts of *C. arvensis* also scavenged DPPH radicals with IC_{50} 51.00–100.00 mg/ml (Kaur et al., 2016). Likewise, *C. prostratus* displayed antioxidant activity with high DPPH scavenging activity (IC_{50}: 14.5–275.0 mg/ml, 100% inhibition; Mathew & Subramanian, 2014; Shahat et al., 2015; Verma et al., 2012), ferrous ion chelating activity (IC_{50}: 14.82 μg/ml), total antioxidant capacity 19.2 mg/ml, and superoxide anion radical scavenging 62.5 μg/ml (Shahat et al., 2015). From the three species reported to possess in vitro antioxidant potency, only *C. prostratus* antioxidant property was confirmed in an animal model. *C. prostratus* showed a neuroprotective effect in Wistar rats and accelerated brain antioxidant defense mechanisms in 3-nitropropionic acid-induced motor deficits and oxidative damage (Kaur et al., 2016). *C. prostratus* was able to reverse the inhibition of the activity or the content of natural antioxidant enzymes like superoxide dismutase (SOD), glutathione (GSH) peroxidase, and reduced GSH within the cortex and hippocampus of scopolamine-induced male Wistar rats that are in the fourth front of the free radicals scavenging defense during oxidative stress (Bihaqi et al., 2011). Scopoletin, a major component of the methanolic extract of *C. prostratus* subfraction, showed significant antioxidant activity in 3-nitropropionic acid-induced Wistar rats by diminishing the high rate of malondialdehyde and nitrite and establishing SOD, and reduced GSH enzyme activity in the cortex and striatum (Kaur et al., 2016).

6 | APPLICATION AS FOOD PRESERVATIVE

The use of plants as food preservatives is gradually growing because of the risk of diseases associated with synthetic additives (Santos-Sánchez, Salas-Coronado, Valadez-Blanco, Hernández-Carlos, & Guadarrama-Mendoza, 2017). Natural antioxidants from plant extracts are widely employed to prevent oxidation and preserve sensory attributes of meat products and represent a promising strategy to extend their shelf life (Nowak, Czyzowska, Efenberger, & Krala, 2016; Ribeiro et al., 2019). Food plants rich in phenolic compounds have been used as sources of antioxidant preservatives. Many authors found a direct correlation between the content of the phenolic compound in the plant such as *C. arvensis* and antioxidant activity and suggested that it could be used as food preservative. In their opinion, the fraction rich in phenolic substances could be used in the food industry (Azman, Husni, Almajano, & Gallego, 2013; Elzaawely & Tawata, 2012; Thakral, Borar, & Kalia, 2010). Indeed, Azman et al. (2015) found that adding 50% ethanol-lyophilized ethanol extracts of *C. arvensis* either as component of the food product or gelatine-based film in active packaging of meat products at a concentration of 0.3% (w/w) prevents lipid oxidation and markedly preserved meat redness and browning color compare with that of synthetic antioxidant, butylated hydroxytoluene (Azman et al., 2015).

7 | TRADITIONAL MEDICINE USE

Convolvulus genus was used in traditional medicine dates back to 1730s. In general, *Concolvulus* plants displayed profuse medicinal uses. Different parts of plant *C. arvensis* have been used as antispasmodic, antiinflammation, antiswelling, treatment for painful joints, treatment against flu, antihemorrhagic, antiangiogenic, laxative, treatment for

TABLE 2 Antimicrobial studies in *Convolvulus* spp

Plant species	Plant part/extract used	Reported activity	Assay method	Target organism	MIC (mg/ml)	References
Convolvulus pilosellifolius Desr.	*Aerial parts/70% ethanol*	Bacteriostatic, fungistatic	*Disc diffusion method*	*Bacillus subtilis*	0.25	(Al-Enazi, 2018; Al-Rifai et al., 2017)
	Aerial parts/95% ethanol		Well-diffusion method	*Pseudomonas aeruginosa*	1.06	
				Escherichia coli	0.93	
				Klebsiella pneumoniae	0.625	
				Proteus vulgaris	0.250	
				Salmonella Typhimurium	31.25	
				Staphylococcus aureus	0.004	
				Staphylococcus epidermidis	0.625	
				Streptococcus pyogenes	1.0	
				Aspergillus fumigatus	0.004	
				Candida albicans	0.156	
				Candida tropicalis	0.156	
				Geotrichum candidum	0.002	
				Microsporum canis	0.004	
				Trichophyton mentagrophytes	1.0	
Convolvulus arvensis L.	*Aerial parts/95% ethanol*	Bacteriostatic, fungistatic	Well-diffusion method	*Escherichia coli*	0.625	(Al-Enazi, 2018; Bazzaz & Haririzadeh, 2003; Borchardt et al., 2008; Edrah et al., 2013; Khan et al., 2015; Miri et al., 2013; Raza et al., 2012; Ullah et al., 2018)
	Leaves and stems/ethanol, methanol, chloroform, acetone, hexane, butanol, ethylacetate, distilled water		Disc diffusion method	*Klebsiella pneumoniae*	0.004	
	Leaf, stem, root/ methanol and fractionated with hexane, chloroform, ethylacetate, butanol, aqueous solvents			*Proteus vulgaris*	0.004	
	Leaf and seed/85% ethanol			*Pseudomonas aeruginosa*	0.019	
	Leaf/aqueous and ethanol			*Bacillus subtilis*	0.004	
				Salmonella Typhimurium	0.078	
				Salmonella paratyphi	0.001	
				Staphylococcus aureus	0.156	
				Staphylococcus epidermidis	0.625	
				Streptococcus pyogenes	0.001	
				Aspergillus fumigatus	0.001	
				Candida albicans	0.078	
				Candida tropicalis	0.001	
				Geotrichum candidum	0.001	
				Microsporum canis	0.156	
				Trichophyton mentagrophytes	NA	
				Acinetobacter junii	NA	
				Acinetobacter baumannii	NA	
				Enterococcus faecalis	NA	
				Shigella dysenteriae	NA	
				Vibrio cholera	NA	
				Proteus mirabilis	NA	
				Serratia marcescens	NA	

(Continues)

TABLE 2 (Continued)

Plant species	Plant part/extract used	Reported activity	Assay method	Target organism	MIC (mg/ml)	References
				Enterobacter cloacae	NA	
				Candida albicans	NA	
				Enterobacter aerogenes	NA	
				Staphylococcus epidermidis	NA	
				Staphylococcus saprophyticus	NA	
Convolvulus prostratus Forssk.	Whole part/methanol	Bacteriostatic	Cup-plate model	*Escherichia coli*	NA	(Singh et al., 2011; Verma et al., 2012)
	Leaves and callus		Agar diffusion method	*Staphylococcus aureus*	NA	
				Bacillus subtilis	NA	

Abbreviations: MIC, minimum inhibitory concentration; NA, not active.

wound, diuretic, antidandruff, and treatment for parasitic infections and jaundice (Ali et al., 2013; Austin, 2008; Dubey, Kumar, & Tripathi, 2004; Gupta, 2005; Leporatti & Ivancheva, 2003; Riordan, Menh, Taylor, & Riordan, 2001). *C. prostratus* is astringent and bitter that can recover the balance and vitiation among three doshas “kapha-vata-pitta” and relieve mental fatigue and stresses (Shah & Bole, 1960). Juice of white-flowered variety of *C. prostratus* is a hallucinogenic remedy for hemicrania. Powder or decoction of *C. prostratus* roots is used to treat ear diseases, rheumatism, chronic bronchitis, fevers, nervous disorders, dysentery, and hair tonic and to normalize high blood pressure (Banjare, Sharma, & Verma, 2014; Hussain, Shah, & Sher, 2007; Rai, 1987). Its laxative, diuretic, emetic, and antiperiodic properties make it effective in the treatment of medical conditions like urinogenital disorders and animal stings (Fantz, 1991). *Concovolvus* plants occupied a prominent position in Ayurvedic medicine, where it has been employed as brain tonic during hypotensive syndromes (Shah & Bole, 1960).

8 | ANTICANCER ACTIVITIES

It has been reported that several members of *Convolvulus* species possessed cytotoxic activity against many tumor cell lines. The antitumor activity of *Convolvulus* species was documented by many in vitro and in vivo studies. The current review will highlight the antitumor activity of *Convolvulus* species (Table 4, Figure 2).

8.1 | *Convolvulus arvensis* L.

Almost all parts of *C. arvensis* possessed an antiproliferative effect on cancer cells. The aqueous and methanolic extracts of leaves, stem, and root of *C. arvensis* as well as its leaves proteoglycan and glycoside extracts showed cytotoxic effects of (78.13–10,000 μg/ml) on human rhabdomyosarcoma (RD) tumor cell line and rat embryo fibroblast (REF-3) cell line in vitro.

Also, the glycoside and proteoglycan extracts were more cytotoxic with a biphasic effect on both cells, a stimulatory effect at low concentrations, and an inhibitory effect at high concentrations after 24 and 48 hr. The glycoside extract showed a significant effect on the mitotic index (MI) of the RD cell line (Al-Asady et al., 2014; Hassan, 2012). *C. arvensis* glycoside extract from leaves showed anticancer activity against RD tumor cell line at 10,000 μg/ml after 72-hr treatment (Al-Asady et al., 2014) through apoptosis, characterized by chromatin condensation, cell volume shrinking, and DNA fragmentation (Al-Asady et al., 2014). A resin glycoside fraction isolated from the alcoholic extract of *C. arvensis* whole plants showed cytotoxic activity (Fan et al., 2018). Chloroform, ethyl acetate, and hydroalcoholic extracts of the aerial parts of *C. arvensis* showed the cytotoxic effect on the human tumor cell line (HeLa, IC_{50} = 15–65 μg/ml) with the chloroform extract having activity comparable with that of taxol (15 vs. 12 μg/ml; Sadeghi-Aliabadi et al., 2008). The 95% alcoholic extract of the aerial parts of *C. arvensis* significantly inhibits the growth of IMR-32 and Colon-205 cell lines by 85% and 73%, respectively (Kaur & Kalia,

TABLE 3 In vitro and in vivo antioxidant activity of different *Convolvulus* plants

Convolvulus spp.	Plant part	In vitro method	In vivo method	Reference
Convolvulus arvensis L.	Whole plant	Nitric oxide scavenging activity	ND	(Khan, Ur-Rehman, Mirza, Ul-Haq, & Zia, 2017)
Convolvulus pilosellifolius Desr.	Aerial parts	DPPH scavenging activity	ND	(Al-Rifai et al., 2017; Ring et al., 2011)
Convolvulus prostratus Forssk.	Leaves, whole plant, aerial parts, roots and aerial part	FRAP, TAC, Fe-chelating, superoxide anion radical scavenging activity, hydrogen peroxide scavenging activity, NQO1 inducer potency	Glutathione peroxidase, inhibition of NADPH oxidation, superoxide dismutase, lipid peroxidation, reduced glutathione in Wistar rats	(Balaji et al., 2014; Bihaqi, Tiwari, & Singh, 2011; Kaur, Prakash, & Kalia, 2016; Mathew & Subramanian, 2014; Shahat, Alsaid, Alyahya, Higgins, & Dinkova-Kostova, 2013; Shahat, Ibrahim, & Alsaid, 2015)

Abbreviations: DPPH, 1,1-diphenyl-2-picrylhydrazyl; FRAP, ferric ion reducing antioxidant potential; NQO1, NAD(P)H-quinoneoxidoreductase; ND, not determined; TAC, total antioxidant capacity.

TABLE 4 In vitro and in vivo anticancer activity of different *Convolvulus* plants

Convolvulus spp.	Plant part	In vitro method	In vivo method	Reference
Convolvulus arvensis L.	Whole plant	Cytotoxic and antitumor activity against various tumor cell lines, acting on mitotic index, inducing apoptosis, and leading to chromatin condensation, cell volume shrinking, and DNA fragmentation	Inhibited angiogenesis in chicken and tumor growth in mice, increased GSH levels, SOD, and CAT enzymes activity, and decreased lipid peroxidation	(Al-Asady, Suker, & Hassan, 2014; Al-Enazi, 2018; Calvino, 2002; Fan et al., 2018; Hassan, 2012; Kaur & Kalia, 2012; Meng et al., 2002; Meng, Riordan, & Riordan, 2000; Sadeghi-Aliabadi, Ghasemi, & Kohi, 2008; Said, 2013; Saleem et al., 2014; Saleem, Naseer, Ahmad, Baig, & Irshad, 2015)
Convolvulus pilosellifolius Desr.	Aerial parts	Antitumor activity against HepG-2, MCF-7, and CACO cells	ND	(Al-Enazi, 2018)
Convolvulus althaeoides L.	Essential oils from fresh flowers	Cytotoxic activity against various tumor cell lines, attributed to the presence of α-humulene, caryophyllene oxide, β-caryophyllene, and germacrene	ND	(Hassine et al., 2014)
Convolvine	Alkaloid from *Convolvulus* spp.	Cytotoxic activity against various cell lines	ND	(Tseomashko et al., 2013)

Abbreviations: CAT, catalase; GSH, glutathione; ND, not determined; SOD, superoxide dismutase.

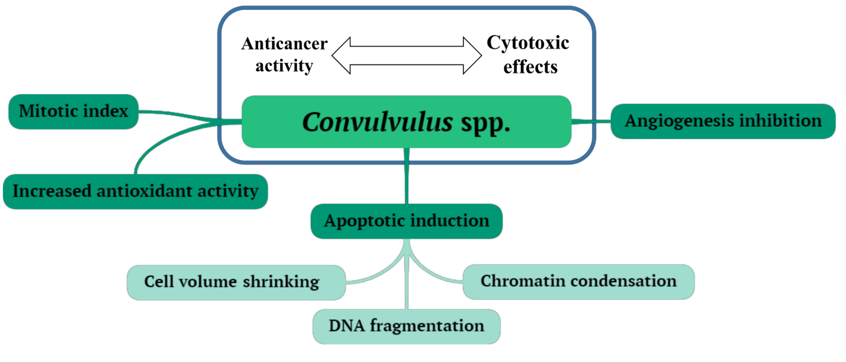

FIGURE 2 *Convulvulus* spp. anticancer mechanisms of action [Colour figure can be viewed at wileyonlinelibrary.com]

2012). The 95% ethanol extract of *C. arvensis* possessed antitumor activity against **hepatocellular carcinoma** (HepG-2, IC_{50} = 6.1 μg/ml), colorectal carcinoma (CACO, IC_{50} = 6.1 μg/ml), breast carcinoma (MCF-7, IC_{50} = 11.1 μg/ml), cervical carcinoma (HeLa, IC_{50} = 17.8 μg/ml), colon carcinoma (HCT-116, IC_{50} = 30.1 μg/ml), prostate carcinoma (Pc3, IC_{50} = 53.3 μg/ml), and lung carcinoma (A-549, IC_{50} = 62.2 μg/ml) (Al-Enazi, 2018). Interestingly, the extract of *C. arvensis* possessed antitumor activity (IC_{50} = 6.1 μg/ml) higher than the antitumor activity of vinblastine sulphate (IC_{50} = 30.3 μg/ml) against CACO (Al-Enazi, 2018).

As well, *C. arvensis* aerial parts extracted with 80% aqueous ethanol and fractionated using petroleum ether, chloroform, ethyl acetate, and *n*-butanol revealed that the chloroform and *n*-butanol fractions significantly decreased MI and increased chromosomal aberrations in a dose of 200 and 400 mg/kg. The petroleum ether only in high doses had significant effects. The ethyl acetate fraction of low dose increased MI and decreased chromosomal aberrations, while the high dose gave the inverse action. The in vitro study showed the inhibited viability of the cultured cell as the concentrations increased, for all the fractions accompanied by the decreased level of TNF-α (Said, 2013).

The ethanol extract of aerial parts of *C. arvensis* decreased the number of living lymphoblastic leukemia, Jurkat cells, in a dose-dependent manner (10–100 μg/ml). This extract induced apoptosis in Jurkat cells especially at 10 μg/ml (85.3%; Saleem et al., 2014).

The primary proteins and polysaccharides extract from *C. arvensis* failed to inhibit the growth of Lewis lung carcinoma (LLC-I) cells and S-I80 mouse sarcoma cells at up to 2 mg/ml but inhibited angiogenesis (Meng et al., 2002). Indeed, the high molecular weight extract of *C. arvensis* has shown the ability to inhibit angiogenesis in chicken chorioallantoin membranes by 73% and at the dose of 14 mg, inhibit tumor growth in mice by 77% (Calvino, 2002; Meng et al., 2002; Sadeghi-Aliabadi et al., 2008). 2 weeks oral administration of the primarily proteins and polysaccharides extract of *C. arvensis* dose-dependently reduced tumor growth in mice, intradermally implanted S-180 sarcoma growth with about 70% at 200 mg/kg/day. Likewise, subcutaneous or intraperitoneal administration of 50 mg/kg/day prevented tumor growth by more than 70% (Meng et al., 2002). The 14 days administration of purified high molecular weight components of *C. arvensis* reduced the tumor size in S-180 fibrosarcoma cells or lung carcinoma cells subcutaneously transplanted to the left inguinal region of mice (74 and 62%, respectively). Furthermore, excised tumors from the treated group contained only 10% tumor tissue and large numbers of lymphocytes and monocytes (Meng et al., 2000).

The crude alkaloids extract from the leaves of *C. arvensis* distracted the microtubule network of a mice cell line (CHO), an invasive metastasis cell after 60 min of exposure in a concentration as little as 20 μg/ml and caused apoptosis at up to 80 and 100 μg/ml (Saleem et al., 2014). The same extract at 1 mg/kg/bw efficiently inhibited CHO cell line tumor growth to 97.1% in mice after 3 weeks of treatment compared with that of untreated control animals (Saleem et al., 2014).

Local application of the methanolic extract of *C. arvensis* at 300 mg/kg/day inhibited the skin tumor incidence up to 20% in 16 weeks in 7-12-dimethyl benz(a)antheracene (DMBA)-induced and croton oil-induced tumor in Swiss albino mice and showed a significant decline in continuous group in cumulative number of papilloma and tumor yield compared with that of carcinogen group. Biochemical investigations showed that the extract increased the levels of GSH, increased the activities of SOD and catalase enzymes, and decreased lipid peroxidation compared with that of carcinogen group (Saleem et al., 2015).

8.2 | *Convolvulus pilosellifolius* Desr.

C. pilosellifolius showed antitumor activity against HepG-2 (IC_{50} = 11.4 μg/ml), MCF-7 (IC_{50} = 15.1 μg/ml), and CACO (IC_{50} = 16.4 μg/ml) cell lines (Al-Enazi, 2018). Interestingly, the extract of *C. pilosellifolius* possessed antitumor activity (IC_{50} = 16.4 μg/ml), respectively, higher than the antitumor activity of vinblastine sulphate (IC_{50} = 30.3 μg/ml) against CACO (Al-Enazi, 2018).

8.3 | *Convolvulus althaeoides* L.

The cytotoxicity of the essential oil from the fresh flowers of the *C. althaeoides* showed cytotoxic activity against human breast cancer cell line with IC_{50} of 8.16 μg/ml. The cytotoxic activity was linked with the presence of anticancer compounds like α-humulene, caryophyllene oxide, β-caryophyllene, and germacrene that are all cytotoxic against breast (MCF-7, MDA-MB-231, Hs 578T), prostate (PC-3), and hepatic (Hep-G2) cancer cell lines (Hassine et al., 2014).

8.4 | Convolvine compound from *Convolvulus* sp.

The activities of alkaloid convolvine, from the genus *Convolvulus*, and its derivatives were studied against HeLa and laryngeal (Hep) cancer cell cultures and primary fibroblast culture. The alkaloid and its derivatives showed potent cytotoxic activity. The alkaloids *N*-benzylconvolvine and *N*-chloroacetylconvolvine at concentrations of 10 μg/ml exhibited the greatest activity against HeLa and Hep cancer cell cultures. The percent suppression of HeLa cervical carcinoma cells and laryngeal cancer cells by alkaloid *N*-benzylconvolvine was 35 and 81.6% (Tseomashko et al., 2013).

9 | CLINICAL EFFECTIVENESS IN HUMANS

Although the use of *Convolvulus* species has a long tradition in folk medicine, especially the application of *C. prostratus* in Ayurveda, the efficacy of these plants has not been studied extensively in human clinical trials. Only two papers report the assessment of preparations containing *Convolvulus* as ingredient.

In a double-blind, randomized, placebo-controlled, cross-over study, the efficacy of a traditional Ayurvedic supplement was studied on 25 volunteers (20 females and 5 males, 20–65 years) suffering from sleep-onset insomnia. The diagnosis of insomnia was established on the bases of subjective complaints of sleep latency, and in a global score >5 on the Pittsburgh Sleep Quality Index, subjects were otherwise healthy. The herbal supplement contained valerian (*Valeriana* *wallichii*; 160 mg/tablet), rose petals (*Rosa centifolia*), muskroot (*Nardostachys jatamansi*), heart-leaved moonseed (*Tinospora cordifolia*), winter cherry (*Withania somnifera*), pepper (*Piper nigrum*), ginger (*Zingiber officinalis*), aloeweed (*C. prostratus*), and licorice root (*Glycyrrhiza glabra*). A 4-night placebo run-in followed by block randomization to either 4 nights placebo or supplement, a 10-day washout, then a cross-over for 4 nights. Patients took either active treatment or placebo, 2 tablets 1 hr before bedtime. As the main outcome measure, sleep latency was measured. The supplement led to a statistically significant decrease in reported sleep latency of 16.7 min (SD = 44.8) as compared with that of placebo. Subjects with longer sleep latency (median split; >45 min) benefited more from the treatment [a mean sleep latency decrease of 28.1 min (SD = 54.9)] than those with shorter sleep latency [decrease 1.91 min (SD = 21.06); $p = .01$]. However, there was no significant change in self-reported difficulty getting off to sleep. There were no self-reported side effects (Farag & Mills, 2003). Although the results reported here are promising, there are several weaknesses of this study. First, the contribution of *Convolvulus* to the overall effect cannot be assessed. Second, the exact composition of the product is not known. Third, compliance was not monitored. Finally, although the appearance of the tablet containing the herbs and placebo was claimed to be identical, the specific odor of valerian might have been a distinctive characteristic.

10 | CONCLUSIONS AND FUTURE PERSPECTIVES

This review covers various aspects of *Convolvulus* plant characteristics, in vitro and in vivo biological activities, and pharmacological properties in traditional medicine. Also, *Convolvulus* plants due its antioxidant and antimicrobial activities have interesting potential as food preservative, that is, preventing lipid oxidation in meat. The majority of the reported properties derived from in vitro assays and a minor number from in vivo studies. Also, clinical trial on *Convolvulus* plant's efficacy is scarce to support claims of efficacy. In vitro anticancer activities need to be supported with in vivo studies and subsequently with clinical studies. It is therefore imperative to confirm the findings by conducting further not only in vivo assays in an animal model but also a clinical trial.

ACKNOWLEDGEMENT

This work was supported by CONICYT PIA/APOYO CCTE AFB170007.

AUTHOR CONTRIBUTIONS

All authors contributed equally to this work. J.S.-R., B.S., M.M., and N. M. critically reviewed the manuscript. All the authors read and approved the final manuscript.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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How to cite this article: Salehi B, Krochmal-Marczak B, Skiba D, et al. *Convolvulus* plant—A comprehensive review from phytochemical composition to pharmacy. *Phytotherapy Research*. 2020;34:315–328. https://doi.org/10.1002/ptr.6540