

Review Article

Antiulcerogenic Activity of *Convolvulus* Species

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Introduction

Family Convolvulaceae contains a large number of important plants which are used in treatment of various diseases elsewhere such as; headache, constipation, rheumatism, diabetes and skin infection [1]. Members of this family mainly contain phenolic, tropane alkaloids [2], flavanoids and coumarins [3]. The largest genus of family Convolvulaceae is *Convolvulus*; it comprises 250 species present as trees, shrubs or herbs [4]. Many *Convolvulus* species are valuable ornamentals, medicinal and food crops [5]. They possess cytotoxic [6], antioxidant, anti-inflammatory and antiulcer activities [3]. In addition they can be used in treatment of coughs and asthma [1].

Peptic ulcer is one of the most common chronic gastrointestinal disorders in modern era. Now it has become a common global health problem affecting a large number of people worldwide and it still a major cause of illness and deaths [7]. There are different classes of drugs are used in the treatment of peptic ulcer, most of them exhibits serious side effects like; arrhythmias, gynaecomastia, arthralgia, hypergastrinemia [8], impotence, haemopoietic changes [7], nausea, abdominal pain, constipation and diarrhea [9].

Plant secondary metabolites have been in use for centuries to cure various ailments. The use of natural medicine in the treatment of peptic ulcer is an absolute requirement of our effort [10]. Traditional medicine has proved to be clinically effective and relatively less toxic than the existing drugs and also reduces the offensive factors serving as a tool in the prevention of peptic ulcer [11].

Plants with anti ulcerogenic activity were used either as raw materials which obtained by extraction with various solvents or as individual isolated compounds. Many solvents have been used to extract active materials from plants such as; alcohol (ethanol or methanol), ether, chloroform, ethyl acetate, n-butanol and water [12].

Abstract

Peptic ulcer disease is one of the most serious gastrointestinal disorders that affect large number of people worldwide and it considered one of the major causes of diseases in the world; because of that it occupies the main position in concern of researchers. The main aim of this article is to search for a safe drug from natural sources, to be used for treatment of ulcers without side effects. Several reports showed that a large number of medicinal plants from *Convolvulus* species possess antiulcer activity in addition to other activities.

Our goal is to collect and compare published data in the last 28 reviews concerning the natural products and the synthetic ones from *Convolvulus* species and other families in the treatment of this disease and other diseases; in addition a quick screening for phytochemical and biological activities of different *Convolvulus* species are reported.

Keywords: Antiulcerogenic activity; *Convolvulus*; Peptic ulcer; Natural products

Peptic ulcer is one of the most serious gastrointestinal disorders which occupy the main position in concern of researchers [13], it can be caused by many factors such as; stress [14], *Helicobacter pylori* [15], acid-pepsin secretion [16], nonsteroidal anti-inflammatory drug [17], cigarettes [18], nutritional deficiencies [19] as well as alcohol [20]. It is a lesion in the gastrointestinal tract that usually occurs in the stomach and duodenum and is characterized by mucosal damage [21].

Natural anti-ulcer products

Peptic ulcer therapy has undergone many steps over the past few years and both herbal and synthetic drugs are now available offering newer and better options for treatment of peptic ulcer [8]. Many synthetic drugs have been used in the treatment of gastric ulcers such as; antacids, anticholinergics, proton pump inhibitors and H₂- receptor antagonists [22]. However, these drugs are expensive [21] and showed an incidence of relapses, drug interactions and side effects [23] thereby limiting their usefulness. The search for an ideal anti-ulcer drug with new and novel molecules has also been extended to herbal drugs and their isolated compounds as alternative ways for treatment of ulcers that afford better protection [24], clinically effective, possess good tolerability even in higher doses [25] and lack of side effects compared to synthetic drugs [26].

Recently, plant extracts are considered to be one of the most attractive sources for developing new drugs and have been shown immense potential results in the treatment of gastric ulcers [27,28]. The literature reported many medicinal plants with antiulcer activity which is used as raw materials (obtained by extraction with solvents) or as individual isolated compounds [29]. Some plants and isolated compounds with antiulcerogenic activity are reported in (Table 1).

Convolvulus species

The *Convolvulus* is a genus of flowering plants in Convolvulaceae family. This genus showed that it contains phenolic, tropane alkaloids

Table 1: An overview of plants with anti-ulcerogenic activity.

Plants	Family	Active Compounds	References
<i>Abarema cochliacarpos</i>	Mimosaceae	(+)-catechins	Silva <i>et al.</i> [30]
<i>Acer tegmentosum</i>	Aceraceae	Salidroside	Yoo <i>et al.</i> [31]
<i>Achillea millefolium</i>	Asteraceae	Total extract	Cavalcanti <i>et al.</i> & Potrich <i>et al.</i> [32,33]
<i>Achyrocline satureioides</i>	Asteraceae	3-O-methylquercetin and luteolin	Santin <i>et al.</i> [22]
<i>Aegle marmelos</i>	Rutaceae	Pyranocoumarin and luvangetin	Goel <i>et al.</i> [34]
<i>Alchornea castaneaefolia</i>	Euphorbiaceae	Total extract	Hiruma-Lima <i>et al.</i> [35]
<i>Alhagi maurorum</i>	Leguminosae	chrysoeriol-7-O-xyloside and kaempferol-3-galactorhamnoside	Awaad <i>et al.</i> [36]
<i>Allophylus serratus</i>	Sapindaceae	quercetin 3-O- β -D-glucuronide and quercetin 3-O-(2"-O-galloyl)-glucoside	Dharmani <i>et al.</i> [37]
<i>Alpinia galangal</i>	Zingiberaceae	1VS-1V-acetoxychavicol acetate and 1VS-1V-acetoxyeugenol acetate	Matsuda <i>et al.</i> [38]
<i>Amomum subulatum</i>	Zingiberaceae	Total extract	Jafri <i>et al.</i> [39]
<i>Anacardium humile</i>	Anacardiaceae	Total extract	Luiz-Ferreira <i>et al.</i> [40]
<i>Anacardium occidentale</i>	Anacardiaceae	Glycosylated quercetin and amentoflavone	Konan <i>et al.</i> [41]
<i>Anogeissus latifolia</i>	Combretaceae	Total extract	Govindarajan <i>et al.</i> [42]
<i>Aparisthium cordatum</i>	Euphorbiaceae	Cordatol, furano-diterpene and aparisthman	Hiruma-Lima <i>et al.</i> [43]
<i>Aralia elata</i>	Araliaceae	Araloside	Lee <i>et al.</i> [44]
<i>Araucaria araucana</i>	Araucariaceae	imbricatolic acid, 15-hydroxyimbricatolal and 15-acetoxyimbricatolic acid	Schmeda-Hirschmann <i>et al.</i> [45]
<i>Argyreia speciosa</i>	Convolvulaceae	Total extract	Jaiswal <i>et al.</i> [46]
<i>Asparagus pubescens</i>	Liliaceae	Total extract	Nwafor <i>et al.</i> [47]
<i>Azadirachta indica</i>	Maliaceae	Total extract	Raji <i>et al.</i> [48]
<i>Baccharis dracunculifolia</i>	Asteraceae	ferulic, <i>p</i> -coumaric and cinnamic acids	Barros <i>et al.</i> [49]
<i>Baccharis trimera</i>	Asteraceae	Total extract	Biondo <i>et al.</i> [50]
<i>Bambusa arundinacea</i>	Graminae	Total extract	Muniappan <i>et al.</i> [51]
<i>Bauhinia purpurea</i>	Fabaceae	Total extract	Zakaria <i>et al.</i> [52]
<i>Bauhinia racemosa</i>	Caesalpiniaceae	Total extract	Borikar <i>et al.</i> [53]
<i>Boswellia serrate</i>	Burseraceae	Boswellic acids	Singh <i>et al.</i> [54]
<i>Byrsonima crassa</i>	Malpighiaceae	quercetin-3-O- β -D-galactopyranoside, quercetin-3-O- α -L-arabinopyranoside, (+)-catechin and (-)-epicatechin	Sannomiya <i>et al.</i> [55]
<i>Byrsonima japurensis</i>	Malpighiaceae	Total extract	Guilhon-Simplicio <i>et al.</i> [56]
<i>Calotropis procera</i>	Apocynaceae	Total extract	Bharti <i>et al.</i> [57]
<i>Campomanesia lineatifolia</i>	Myrtaceae	Total extract	Madalosso <i>et al.</i> [58]
<i>Campomanesia xanthocarpa</i>	Myrtaceae	Total extract	Markman <i>et al.</i> [59]
<i>Capsicum annuum</i>	Solanaceae	Capsaicin	Kanget <i>et al.</i> [60]
<i>Cardiospermum halicacabum</i>	Sapindaceae	Total extract	Sheeba <i>et al.</i> [61]
<i>Casearia sylvestris</i>	Flacourtiaceae	Total extract	Esteves <i>et al.</i> [62]
<i>Cedrus deodara</i>	Pinaceae	Total extract	Kumar <i>et al.</i> [63]
<i>Centaurea helenioides</i>	Asteraceae	grosheimin and cynaropicrin	Yayli <i>et al.</i> [64]
<i>Centella asiatica</i>	Apiaceae	Total extract	Cheng <i>et al.</i> & Abdullah <i>et al.</i> [65,66]
<i>Cinnamomum tamala</i>	Lauraceae	Total extract	Eswaran <i>et al.</i> [67]
<i>Cissus sicyoides</i>	Vitaceae	Total extract	Ferreira <i>et al.</i> [68]
<i>Cissus quadrangularis</i>	Vitaceae	Total extract	Jainu <i>et al.</i> & Austin <i>et al.</i> [69,70]
<i>Citrus aurantium</i>	Rutaceae	Limonene	Moraes <i>et al.</i> [71]
<i>Citrus lemon</i>	Rutaceae	limonene and β -pinene	Rozza <i>et al.</i> [72]
<i>Cocos nucifera</i>	Arecaceae	Total extract	Anosike & Obidoa <i>et al.</i> [73]
<i>Cordia verbenacea</i>	Boraginaceae	Total extract	Roldao <i>et al.</i> [74]
<i>Croton cajucara</i>	Euphorbiaceae	Total extract	Almeida <i>et al.</i> & De Paula <i>et al.</i> [75,76]
<i>Cyclea peltata</i>	Menispermaceae	Total extract	Shine <i>et al.</i> [77]
<i>Cynanchum auriculatum</i> and <i>Cynanchum bungei</i>	Asclepiadaceae	Total extract	Shan <i>et al.</i> [78]
<i>Da-illa rugosa</i> Poiret	Dilleniaceae	Total extract	Guaraldo <i>et al.</i> [79]
<i>Decalepis hamiltonii</i>	Asclepiadaceae	Total extract	Naik <i>et al.</i> [80]
<i>Desmostachia bipinnata</i>	Gramineae	trycinand trycin-7-glucoside	Awaad <i>et al.</i> [81]
<i>Dioscorea oppositifolia</i>	dioscoreaceae	Total extract	Jhansirani <i>et al.</i> [82]
<i>Dodonaea viscosa</i>	Sapindaceae	Total extract	Arun <i>et al.</i> [83]

<i>Elettaria cardamomum</i>	Zingiberaceae	Total extract	Jamal <i>et al.</i> [84]
<i>Emblica officinalis</i>	Euphorbiaceae	Total extract	Sairam <i>et al.</i> [85]
<i>Enantiachlorantha</i>	Annonaceae	7,8-dihydro-8-hydroxypalmatine	Tan & Nyasse <i>et al.</i> [86]
<i>Eqiusetum palustre</i>	Equisetaceae	kaempferol-3-O-1"-β-D-glucopyranosyl-3-O-1"-β-D-glucopyranoside	Gurbuz <i>et al.</i> & Yesilada <i>et al.</i> [87,88]
<i>Excoecaria agallocha</i>	Euphorbiaceae	Total extract	Thirunavukkarasu <i>et al.</i> [89]
<i>Fabiana imbricate</i>	Solanaceae	11-hydroxy-4-amorphen-15-oic acid and Oleanolic acid	Reyes <i>et al.</i> & Sanchez <i>et al.</i> [90,91]
<i>Ficus glomerata</i>	Moraceae	Total extract	Rao <i>et al.</i> [92]
<i>Ficus religiosa</i>	Moraceae	Total extract	Khan <i>et al.</i> [9]
<i>Galipea longiflora</i>	Rutaceae	alkaloid extract and 2-phenylquinoline	Zanatta <i>et al.</i> [93]
<i>Garcinia kola</i>	Clusiaceae	Kolaviron	Olaleye <i>et al.</i> [94]
<i>Glycyrrhiza glabra</i>	Fabaceae	Total extract	Wittschier <i>et al.</i> [95]
<i>Guiera senegalensis</i>	Combretaceae	1,3-digalloylquinic acid and 5-methylidihydroflavasperone	Aniagu <i>et al.</i> [96]
<i>Hedyotis puberula</i>	Rubiaceae	Total extract	Joseph <i>et al.</i> [97]
<i>Hyptis martiusii</i>	Lamiaceae	Total extract	Caldas <i>et al.</i> [21]
<i>Hyptis spicigera</i>	Lamiaceae	alpha-pinene, cineole and beta-pinene	Takayama <i>et al.</i> [98]
<i>Jasminum grandiflorum</i>	Oleaceae	Total extract	Umamaheswari <i>et al.</i> [99]
<i>Jatropha isabelli</i>	Euphorbiaceae	jatrophone, jatrophone A and B and 9β,13α-dihydroxyisabellione	Pertino <i>et al.</i> [100]
<i>Kielmeyera coriacea</i>	Guttiferae	Total extract	Goulart <i>et al.</i> [101]
<i>Lantana camara</i>	Verbenaceae	Verbascoside and umuhengerin	Sathish <i>et al.</i> [102]
<i>Lippia sidoides</i>	Verbenaceae	Essential oil	Monteiro <i>et al.</i> [103]
<i>Mangifera indica</i>	Anacardiaceae	Total extract	Lima <i>et al.</i> [104]
Many plants	-	Total extract	Atta <i>et al.</i> [105]
Many plants	-	Total extract	Dharmani & Palit <i>et al.</i> [106]
<i>Maytenus aquifolium</i> , <i>Sorocea bomplandii</i> and <i>Zolernia ilicifolia</i>	Celastraceae, Moraceae and Fabaceae	Total extract	Gonzalez <i>et al.</i> [107]
<i>Maytenus ilicifolia</i>	Celastraceae	friedelan-3β-ol, friedelin and polygalacturonic acid	Queiroga <i>et al.</i> , Jorge <i>et al.</i> , Baggio <i>et al.</i> & Cipriani <i>et al.</i> [108-110]
<i>Maytenus robusta</i>	Celastraceae	3,15-dioxo-21-α-hydroxyfriedelane	Andrade <i>et al.</i> [111,112]
<i>Melanthera scandens</i>	Compositae	Total extract	Okokon <i>et al.</i> [113]
<i>Mentha piperita</i>	Lamiaceae	Total extract	Al-Mofleh <i>et al.</i> [114]
<i>Momordica charantia</i>	Cucurbitaceae	Total extract	Alam <i>et al.</i> [115]
<i>Morinda citrifolia</i>	Rubiaceae	Total extract	Mahattanadul <i>et al.</i> [116]
<i>Moringa oleifera</i>	Moringaceae	Total extract	Debnath <i>et al.</i> [117]
<i>Morus alba</i>	Moraceae	Total extract	Abdulla <i>et al.</i> [118]
<i>Mouriri pusa</i>	Melastomataceae	Total extract	Vasconcelos <i>et al.</i> [119,120]
<i>Myristica malabarica</i>	Myristicaceae	Malabaricone and omeprazole	Banerjee <i>et al.</i> [121]
<i>Ocimum sanctum</i>	Labiatae	Total extract	Dharmani <i>et al.</i> [122]
<i>Olox subscorpioidea</i>	Olacaeae	Total extract	Victoria <i>et al.</i> [123]
<i>Opuntia ficus indica</i>	Cactaceae	Total extract	Galati <i>et al.</i> & Alimi <i>et al.</i> [124,125]
<i>Oroxylum indicum</i>	Bignoniaceae	flavonoid glycosides	Babu <i>et al.</i> [126]
<i>Panax ginseng</i>	Araliaceae	Ginsenoside Rb1	Jeong <i>et al.</i> & Sun <i>et al.</i> [127,128]
<i>Papaver somniferum</i>	Papaveraceae	Morphine	Tazi-Saad <i>et al.</i> [129]
<i>Piper betel</i>	Piperaceae	phenol, allylpyrocatechol	Yadav <i>et al.</i> & Bhattacharya <i>et al.</i> [130,131]
<i>Plectranthus grandis</i>	Lamiaceae	Barbatusin, 3β-hydroxy-3-deoxybarbatusin and diterpenes	Rodrigues <i>et al.</i> [132]
<i>Plinia edulis</i>	Myrtaceae	Total extract	Ishikawa <i>et al.</i> [133]
<i>Pradosia huberi</i>	Sapotaceae	Total extract	Kushima <i>et al.</i> [134]
<i>Prumnopitys andina</i>	Podocarpaceae	Ferruginol	Rodriguez <i>et al.</i> [135]
<i>Pteleopsis suberosa</i>	Combretaceae	Total extract	German <i>et al.</i> [136]
<i>Pterocarpus santalinus</i>	Fabaceae	Total extract	Narayan <i>et al.</i> [137]
<i>Qualea grandiflora</i>	Vochysiaceae	Total extract	Hiruma-Lima <i>et al.</i> [35]
<i>Quassia amara</i>	Simaroubaceae	Total extract	Garcia-Barrantes <i>et al.</i> [138]
<i>Raphinus sativus</i>	Cruciferae	Total extract	Devaraj <i>et al.</i> [139]
<i>Rhizophora mangle</i>	Rhizophoraceae	Total extract	Perera <i>et al.</i> & De-Faria <i>et al.</i> [19,140]
<i>Sapindus saponaria</i>	Sapindaceae	Total extract	Albiero <i>et al.</i> [141]
<i>Scoparia dulcis</i>	Scrophulariaceae	Total extract	Babincova <i>et al.</i> & Mesia-vel <i>et al.</i> [142,143]

<i>Scutellaria baicalensis</i>	Lamiaceae	Wogonin	Park <i>et al.</i> [144]
<i>Senecio candicans</i>	Asteraceae	Total extract	Lakshmanan <i>et al.</i> [145]
<i>Simaba ferruginea</i>	Patellidae	Canthin-6-one	Almeida <i>et al.</i> [146]
<i>Solanum aethiopicum</i>	Solanaceae	Total extract	Chioma <i>et al.</i> [147]
<i>Solanum nigrum</i>	Solanaceae	Total extract	Jainu <i>et al.</i> [148]
<i>Solidago chilensis</i>	Asteraceae	Solidagenone	Schmeda-Hirschmann <i>et al.</i> [149]
<i>Strychnos potatorum</i>	Loganiaceae	Total extract	Sanmugapriya <i>et al.</i> [150]
<i>Strychnos pseudoquina</i>	Loganiaceae	Total extract	Bonamin <i>et al.</i> [151]
<i>Syagrus oleracea</i>	Arecaceae	galactomannoglucan	Silva <i>et al.</i> [152]
<i>Terminalia arjuna</i>	Combretaceae	Total extract	Devi <i>et al.</i> [153]
<i>Terminalia belerica</i>	Combretaceae	gallic acid	Bhattacharya <i>et al.</i> [154]
<i>Terminalia pallida</i>	Combretaceae	Total extract	Gupta <i>et al.</i> [155]
<i>Trichosanthes cucumerina</i>	Cucurbitaceae	Total extract	Arawwawala <i>et al.</i> [156]
<i>Trigonella foenum-graecum</i>	Fabaceae	Total extract	Pandian <i>et al.</i> [157]
<i>Usnea longissima</i>	Parmeliaceae	Usnic acid	Odabasoglu <i>et al.</i> [158]
<i>Utleria salicifolia</i>	Periplocaceae	Total extract	Rao <i>et al.</i> [159]
<i>Vernonia polyanthes</i>	Compositae	Total extract	Barbastefano <i>et al.</i> [160]
<i>Virola surinamensis</i>	Myristicaceae	epicatechin	Hiruma-Lima <i>et al.</i> [161]
<i>Xylocarpus granatum</i>	Meliaceae	Total extract	Lakshmi <i>et al.</i> [162]
<i>Ya-hom</i>	many plants	Total extract	Suvitayavat <i>et al.</i> [163]
<i>Zanthoxylum rhoifolium</i>	Rutaceae	Total extract	Freitas <i>et al.</i> [164]
<i>Zingiber officinale</i>	Zingiberaceae	6-gingerol and 6-shogaol	Wang <i>et al.</i> , Minaiyan <i>et al.</i> & Anosik <i>et al.</i> [165-167]
<i>Zizyphus lotus</i>	Rhamnaceae	Total extract	Wahida <i>et al.</i> [168]
<i>Zizyphus oenoplia</i>	Rhamnaceae	Total extract	Jadhav <i>et al.</i> [169]

[169], sterols, resin and sugars [170]. It has been reported that it exhibits many activities such as; asthma, jaundice [171], cytotoxic effects [172], anti-cancer activity [173] and antioxidant activity [169]. Although nothing was traced about the plant under investigation, reviewing the current literature there are many of the species of this genus were studied for their biological activity and isolated compounds.

Phytochemical contents of *Convolvulus* species: Studies showed that the convolvulus species contains phenolics [174], saponins, steroids, alkaloids, proteins, lipids [175], polyphenolic compounds [5], flavonoid [11,176], coumarins [177,178], volatile oil, carbohydrates [179], tannins, cardiac glycosides [180,181], triterpenoids [182], lactones and amino acids [183].

Biological activities of *Convolvulus* species: Reviewing the previous literatures; we found that *Convolvulus* species possess various biological activities such as; cytotoxic activity, stimulating effects [175], antimicrobial activity [184], anticonvulsant activity, antioxidant activity [1,176,185], neuroprotective effect [186], antimicrobial activity [187,178], anti-inflammatory, anti-nociceptive, antipyretic activities [11], laxative effect [5], scavenging activity [169], antibacterial, antiulcer [177], antistress [177], antidysenteric, hypolipidaemic, larvicidal, anti-mosquito properties and useful as a memory enhancer [182], antidiarrhoeal effect [183], anti-cancer agents [188], anti-angiogenesis [172], CNS-depressant activity [189], antifeedant [182], antidiabetic activity [190] and inhibition of platelet aggregation [191].

Isolated compounds from *Convolvulus* species: Many compounds have been isolated and reported in literatures from *Convolvulus* species such as; *p*-hydroxybenzoic acid, syringic acid and vanillin [174], quercetin, quercetin 3-O-rutinoside and quercetin-7-O-rhamnoside, ferulic acid [1], *p*-coumaric acid [192],

3-(2-butoxy-3-caffeoyl-1-hydroxycyclobutyl)-3-hydroxypropanoic acid and 4-O-(4'-carboxymethyl-2',4',6'-trihydroxycyclohexyl) vanillic acid [169], scopoletin, β -sitosterol and ceryl alcohol [177], Phytosterol [179], cuscohygrine [193], choline hydrochloride, betain hydrochloride [178], umbeliferone, asculetin, scopoline, kaempferol-3-rhamnoside [194], 29-oxodotriacontanol, tetratriacontanoic acid [182], Pseudotropine and hygrine [173].

MEDLINE Search

To collect the data which support this idea we performed a systematic review using PubMed, Google, Science direct and MEDLINE database. All English-language articles published between 1964 and 2012 were searched using the terms 'antiulcerogenic', 'anti-ulcer', 'gastroprotective', 'gastric antiulcerogenic', 'peptic ulcer', '*Convolvulus*', 'natural products', '*Helicobacter pylori*', 'plant extracts', 'synthetic anti-ulcer compounds'. Plants names, families and authorities were confirmed using <http://www.tropicos.org/> and <http://www.theplantlist.org/> sites.

Conclusion

Peptic ulcer can be considered as the most wide distributed diseases and a lot of work has been reported in literature talking about this disease. *Convolvulus* family contains many species mentioned in literature have a high biological activity as anti-ulcerogenic. Some researcher used the total extract in treatment of ulcer; others studied the effect of the isolated compounds.

Reviewing the last 28 years, many researchers from different countries focused on the scientific proof of the activity of this family species. Scientists found that the amount extracted from natural sources is too much little to be economically benefited in industrial or medicinal fields, so they try to mimic the isolated natural compounds synthetically, studying the biological activity and the side effects of the synthetic compounds.

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