

Review Article

# A Perspective on therapeutic potential of weeds

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## Abstract

Nature gives us a diverse plethora of floral wealth. Weeds have been recognized as invasive plant by most of scholars in today's world with extraordinary travel history. They are considered to be noxious for adjoining plant species and also as economic hazard. Weeds inhabited in almost entire biomes and have capability to survive in harsh conditions of environment thereby become source of inspiration for finding novel phytoconstituents. Weeds play a significant role in absorbing harmful micro pollutants that are affecting ecosystem adversely. There are so many examples like canna lily, bladder wort, coltsfoot, giant buttercup etc. playing crucial part in sustaining environment. Different isolation and characterization approaches like high pressure liquid chromatography, gas chromatography, ion exchange chromatography, nuclear magnetic resonance, mass spectroscopy etc. have also been fetched for obtaining novel constituents from weeds. The main aim of this review is to analyze the therapeutic potential of weeds established in New Zealand and effort to unfold the wide scope of its applications in biological sciences. Upon exploration of various authorized databases available it has been found that weeds not only are the reservoir of complex phytoconstituents exhibiting diverse array of pharmacological activities but also provide potential role in environment phytoremediation. Phytoconstituents reported in weeds have immense potential as a drug targets for different pathological conditions. This review focuses on the literature of therapeutic potential of weeds established in New Zealand and tried to unveil the hidden side of these unwanted plants called weeds.

## Introduction

'Horse Hoeing Husbandry' named famous writing by Jethro Tull (1731) mentioned first time the word 'weed' [1]. Weeds may be considered as plants whose abundance must be over or above a specific level can cause major environmental concern [2]. Aldrich and Kremer, 1997 defined weed as a part of dynamic ecosystem [3]. Plant originated in natural environment and, in response to imposed or natural environments, evolved, and continues to do so, as an interfering associate with crops and activities. Weeds may interfere with the utilization of land and water resources thereby adversely affect human welfare [4]. According to Ancient Indian Literature earth is blessed with diverse flora and every existing plant has their own importance. Some plants are considered unwanted but they may have beneficial properties. Scholars are trying hard to explore the hidden potential of such unwanted plants [5]. Weeds have interactions with other organisms and some of these interactions can have direct effects on the functioning of agro-ecosystem [6]. They serve as an indirect resource for predatory species [7] and it could alternative food sources for organisms that play prominent role in insect control [8]. Weeds have a unique travel history. Clinton L. Evans in his

book 'The war on weeds in the prairie west- An Environmental History' mentioned about travelling of weeds in ships, railways, automobiles from one country to another as food contaminants, animal feed, farm implements etc. during trade [9]. Weeds are firmly distributed and established all over New Zealand. Authors Ian Popay, Paul Champion and Trevor James in their book 'An Illustrated Guide to Common Weeds of New Zealand' (edition 3<sup>rd</sup>) published by New Zealand Plant Protection Society in 2010 mentioned the detailed description of around 380 weed species established in New Zealand [10]. Different scientific databases/ information resources (governmental, private, universities, initiatives, organizations etc.) of New Zealand extensively explored over a year as mentioned in table 1 to obtain data pertaining to weeds prevalent within geographical boundaries of New Zealand. After obtaining desired data of different weeds, a literature search was performed using the keyword "Name of weed (e.g. *Aristea ecklonii*) Pharmacology", "New Zealand plants", "weed pharmacology", "therapeutic weed" individually or all together in different scientific databases of Scopus, Web of Science and Pubmed to obtain therapeutic potential of weeds. *Celastrus orbiculatus* (Climbing spindle berry) [59], *Robinia pseudoacacia* (False acacia) [63], *Daphne laureola*

## More Information

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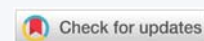
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**Table 1:** Description of scientific databases/ information resources of New Zealand for weed identification.

PRIMARY INFORMATION SOURCES			SECONDARY INFORMATION SOURCES*	
Source name	Source type	Authors	Web address	Database/information resource
An encyclopedia of New Zealand, 1966	Encyclopedia	McLintock AH	<a href="http://www.agpest.co.nz">http://www.agpest.co.nz</a>	AgPest: It is an open access tool available for New Zealand farmers and agricultural professionals containing information about weeds, pest identification, their biology, impact and management
Common weeds in New Zealand, 1976	Book	Parham BEV, Healy AJ	<a href="http://www.agriculture.vic.gov.au">http://www.agriculture.vic.gov.au</a>	Agriculture victoria : Platform is used to promote agriculture industry in New Zealand and encompass information related to weeds and plant protection
Weeds in New Zealand protected natural areas: A review for the Department of Conservation, 1990	Book	Williams PA, Timmins SM	<a href="http://www.cropscience.bayer.co.nz">http://www.cropscience.bayer.co.nz</a>	Bayer crop science: It is one of the major information providers of crop protection products
Problem weeds on New Zealand islands, 1997	Book ISBN 0-478-01885-1	Atkinson IAE	<a href="http://www.gw.govt.nz">http://www.gw.govt.nz</a>	Greater wellington university: It is a local government body in New Zealand represented by regional and territorial councils
New Zealand Journal of Agricultural Research, 50(2), 2007	Journal	Bourdote GW, Fowler SV, Edwards GR, Kriticos DJ, Kean JM, Rahman A, Parsons AJ	<a href="http://www.learnz.org.nz">http://www.learnz.org.nz</a>	Learnz: It is a initiative of free virtual field trips that help students to acquire inaccessible knowledge regarding various agricultural activities
Consolidated list of environmental weeds in New Zealand, 2008	Journal ISBN 978-0-478-14412-3	Howell C	<a href="http://www.massey.ac.nz">http://www.massey.ac.nz</a>	Massey university: In Massey University, College of Sciences prepared a database dedicated to provide information regarding weeds in New Zealand
New Zealand Journal of Ecology, 33 (2), 2009	Journal	Sullivan JJ, Williams PA, Timmins SM, Smale MC	<a href="http://www.mpi.govt.nz">http://www.mpi.govt.nz</a>	Ministry for primary industries: The Ministry for Primary Industries is dedicated to improving agriculture productivity, food safety, increasing sustainability and reducing biological risk
An illustrated guide to common weeds of New Zealand, 2010	Book	Popay I, Champion P, James T	<a href="http://www.nzpcn.org.nz">http://www.nzpcn.org.nz</a>	New Zealand plant conservation network: This network system is framed to conserve the floral wealth of New Zealand
New Zealand Journal of Ecology, 39(1), 2015	Journal	McAlpine KG, Lamoureaux SL, Westbrooke I	<a href="http://www.ourbigbackyard.nz">http://www.ourbigbackyard.nz</a>	Our big backyard: This aims to restore, create and maintain healthy habitats of New Zealand
Agronomy, 9, 2019	Journal	Ghanizadeh H, Harrington KC	<a href="http://www.waikoregion.govt.nz">http://www.waikoregion.govt.nz</a>	Waikato: This local government body works for maintaining agriculture resources and sustainability to ensure strong economy
Climate change risk assessment for terrestrial species and ecosystems in the Auckland region. Auckland Council, 2019	Technical report ISBN 978-1-98-858966-4	Bishop C, Landers TJ	<a href="http://www.weedbusters.org.nz">http://www.weedbusters.org.nz</a>	Weedbusters: Programme facilitates to eradicate weeds in New Zealand

\*Secondary information resources/databases have been explored from March 2019 to March 2020

(Green daphne laurel) [66], *Glaucium flavum* (Horned poppy) [70], *Senecio latifolius* (Pink ragwort) [80], *Solanum nigrum* (Black night shade) [86] have potent anticancer activities. *Aristea ecklonii* (Aristea) [50], *Alocasia brisbanensis* (Elephant ear) [62], *Lycopus europaeus* (Gypsywort) [68] exhibited antimicrobial activities. *Pseudosasa japonica* (Arrow bamboo) [51], *Sambucus nigra* (Elder) [61], *Equisetum arvense* (Field horsetail) [65] showed antioxidant effect. *Hedera helix* (Ivy) [72], *Nymphaea Mexicana* (Mexican water lily) [75], *Persicaria hydropiper* (Water pepper) [106] showed anti-inflammatory properties. Weeds like *Zantedeschia aethiopica* (Arum lily) [112], *Utricularia gibba* (Bladderwort) [113], *Canna indica* (Canna lily) [114], *Tussilago farfara* (Coltsfoot) [115], *Egeria densa* (Eregia) [116], *Ranunculus acris* (Giant buttercup) [117], *Cytisus scoparius* (Broom) [118], *Poa annua* (Annual poa) have prominent role in biomonitoring of heavy metals in multiple environments [119].

### Chemical profile of weeds established in New Zealand

Weeds established in New Zealand encompass wide array of therapeutic phytoconstituents. Weeds serve as biosynthetic

factory for synthesis of phytochemicals. They are sources of rich medicinal wealth which includes primary metabolites (polysaccharides) and secondary metabolites (alkaloids, flavonoids, glycosides, tannins, volatile oils etc.). They are the potential sources of complex phytoconstituents. *Selaginella kraussiana* (African club moss) [11], *Lonicera japonica* (Japanese honeysuckle) [32], *Eriobotrya japonica* (Loquat) [35] and *Anredera cordifolia* (Mignonette vine) [38] contains polysaccharides. *Alternanthera philoxeroides* (Alligator weed) [13] and *Rhamnus alaternus* (Evergreen buckthorn) [26] contains anthraquinone glycosides. *Lamium galeobdolon* (Artillery plant) [14] and *Heracleum mantegazzianum* (Giant hogweed) [27] contains appreciable amount of volatile oil. Modern spectroscopic methods have been explored for structural elucidation of bioactive constituents present in weeds. LC-MS has been used for quantitative detection of xyloglucan oligosaccharide in *Selaginella kraussiana* [11], betulonic acid in *Alnus glutinosa* (Black alder) [12], jasmonic acid in *Drosera capensis* (Cape sundew) [20], flavonoids in *Gunnera tinctoria* (Chilean rhubarb) [24], pyrrolizidine alkaloid esters in *Gymnocoronis spilanthoides* (Senegal tea)

[42]. NMR employed for characterization of compounds present in *Fraxinus excelsior* (Ash) [15], *Berberis glaucocarpa* (Barberry) [17], *Ligustrum sinense* (Chinese privet) [25], *Rhamnus alaternus* [26], *Cestrum parqui* (Green cestrum) [30], *Ranunculus sardous* (Hairy buttercup) [49]. Detailed summary of chemical compounds isolated from weeds established in New Zealand indicated in table 2.

### Therapeutic potential of weeds established in New Zealand

Weeds have been explored for diverse pharmacological actions like anti cancer, anti microbial, anti-inflammatory, antioxidant, antiviral etc. as mentioned in table 3 and figure 1.

**Anticancer weeds:** Some important cytotoxic weeds

**Table 2:** A summary of compounds isolated from weeds established in New Zealand.

Common name	Botanical name	Native of	Compound reported	Analytical approach adopted	References
African club moss	<i>Selaginella kraussiana</i> Selaginellaceae	Africa	Xyloglucan oligosaccharide	Matrix assisted laser desorption ionization time of flight (MS), high performance anion exchange chromatography	[11]
Black alder	<i>Alnus glutinosa</i> Betulaceae	Eurasia, Africa	Betulin, betulonic acid, betulonic acid, lupeol	Desorption atmospheric pressure photoionization (MS)	[12]
Alligator weed	<i>Alternanthera philoxeroides</i> Amaranthaceae	South America	Anthraquinone glycosides	Spectral analysis	[13]
Artillery plant	<i>Lamium galeobdolon</i> Lamiaceae	Europe, Asia	Volatile compounds	GC-MS	[14]
Ash	<i>Fraxinus excelsior</i> Oleaceae	Europe, Asia, Africa	Nodulisporiviridin M	ID, 2D 1H & 13C NMR	[15]
Asiatic knotweed	<i>Fallopia japonica</i> Polygonaceae	Asia	Carotenoid	HPTLC, HPLC-MS	[16]
Barberry	<i>Berberis glaucocarpa</i> Berberidaceae	Himalayas	Bisbenzylisoquinoline alkaloid, oxyacanthine	1D, 2D NMR	[17]
Blackberry	<i>Rubus fruticosus</i> Rosaceae	North temperate regions	Polyunsaturated fatty acids	Supercritical carbon dioxide method	[18]
Boxthorn	<i>Lycium ferocissimum</i> Solanaceae	South Africa	Betaine	Fast atom bombardment mass spectroscopy	[19]
Cape sundew	<i>Drosera capensis</i> Droseraceae	South Africa	Jasmonic acid	LC-MS/MS	[20]
Castor oil	<i>Ricinus communis</i> Euphorbiaceae	Africa, Eurasia	Ricin	Spectral analysis	[21]
Century plant	<i>Agave americana</i> Agavaceae	Mexico	Fructans	Thermogravimetric analysis	[22]
Cherry laurel	<i>Prunus laurocerasus</i> Rosaceae	South East Europe	Cyanogenetic glycosides, benzoic acid derivative	LC-ESIMS	[23]
Chilean rhubarb	<i>Gunnera tinctoria</i> Gunneraceae	South America	Flavonoids	HPLC-MS/MS	[24]
Chinese privet	<i>Ligustrum sinense</i> Oleaceae	China	10-hydroxyl-oleuropein, 3-O-alpha-L-rhamnopyranosyl-kaempferol-7-O-beta-D-glucopyranoside	1D, 2D NMR	[25]
Evergreen buckthorn	<i>Rhamnus alaternus</i> Rhamnaceae	Mediterranean region	Anthraquinone glycosides	1D, 2D NMR, FAB-MS	[26]
Giant hogweed	<i>Heracleum mantegazzianum</i> Apiaceae	Eurasia	Essential oil	GC-MS	[27]
Giant knotweed	<i>Fallopia sachalinensis</i> Polygonaceae	Asia	Olymeric procyanidins, flavones, flavonoids	GC-MS	[28]
Giant reed	<i>Arundo donax</i> Gramineae	Eurasia	Bis-indole alkaloid, phenylpropanoid	Spectral analysis	[29]
Green cestrum	<i>Cestrum parqui</i> Solanaceae	Chile, Peru	Saponin	1H, 13C NMR	[30]
Heather	<i>Calluna vulgaris</i> Ericaceae	Europe	Catechin, epicatechin	HPLC-DAD-ESI/MS	[31]
Japanese honeysuckle	<i>Lonicera japonica</i> Caprifoliaceae	Japan	Polysaccharides	HPLC, FTIR	[32]
Khasia berry	<i>Cotoneaster simonsii</i> Rosaceae	China	Tocopherols	Spectral analysis	[33]
Kudzu vine	<i>Pueraria lobata</i> Fabaceae	Japan	Lobatamunsolides A-C, norlignans	LC-MS	[34]
Loquat	<i>Eriobotrya japonica</i> Rosaceae	China, Japan	Polysaccharides	UMAE	[35]
Manchurian rice grass	<i>Zizania latifolia</i> Poaceae	China	Proanthocyanidins	UAE	[36]
Mexican devil	<i>Ageratina adenophora</i> Asteraceae	South America	Thymol derivatives	1H NMR, HR-ESI-MS, IR	[37]



Mignonette vine	<i>Anredera cordifolia</i> Basellaceae	South America	Water soluble polysaccharides	UV, FTIR	[38]
Moth plant	<i>Araujia hortorum</i> Asclepiadaceae	Brazil, Argentina	Protease (araujain)	Ultracentrifugation, ion exchange chromatography, MS	[39]
Mysore thorn	<i>Caesalpinia decapetala</i> Fabaceae	Asia	Cassane type furanoditerpenoids	HPLC, 1D NMR, 2D NMR, HRESIFTMS	[40]
Plectranthus	<i>Plectranthus ciliates</i> Lamiaceae	South Africa	Anthocyanins	UV	[41]
Senegal tea	<i>Gymnocoronis spilanthoides</i> Asteraceae	Mexico	Pyrrrolizidine alkaloid esters	HPLC, MS-MS	[42]
Tree of heaven	<i>Ailanthus altissima</i> Simaroubaceae	China	Phenylpropanoids	NMR, HRESIMS	[43]
Tuber ladder fern	<i>Nephrolepis cordifolia</i> Davalliaceae	Australia	2,4-hexadien-1-ol, nonanal, thymol	GC-MS	[44]
White bryony	<i>Bryonia cretica</i> Cucurbitaceae	Eurasia	Cucurbitane type triterpene	Bioassay guided fractionation, NMR	[45]
Bracken	<i>Pteridium esculentum</i> Dennstaedtiaceae	Australia	Ptesculentoside, caudatoside, ptaquiloside	LC-MS	[46]
Catsear	<i>Hypochaeris radicata</i> Asteraceae	Eurasia	Lignans, sesquiterpene lactones	NMR, HRMS	[47]
Creeping buttercup	<i>Ranunculus repens</i> Ranunculaceae	Europe, Asia	Methyl 3,4,5-trihydroxybenzoate	1D, 2D NMR	[48]
Hairy buttercup	<i>Ranunculus sardous</i> Ranunculaceae	Europe, Asia	Ranunculin	TLC, HPTLC	[49]

**Table 3:** A summary of pharmacological activities exhibited by weeds.

Common name	Botanical name	Native of	Reported pharmacological activity	Outcome of study	Reference
Aristea	<i>Aristea ecklonii</i> Iridaceae	West and South Africa	Antimicrobial	Plumbagin isolated from plant exhibited antimicrobial activities with MIC 2 µg/ml and 16 µg/ml	[50]
Arrow bamboo	<i>Pseudosasa japonica</i> Poaceae	Japan, South Korea	Antioxidant	Leaves extract has potential to ameliorate oxidative stress by improving antioxidant activity	[51]
Bear's breeches	<i>Acanthus mollis</i> Acanthaceae	South West Europe	Antioxidant, anti-inflammatory	Ethanol extract inhibited NO production	[52]
Blue spur flower	<i>Plectranthus ecklonii</i> Lamiaceae	South Africa	Against pancreatic cancer	Antiproliferative effect was found to be effective against BxPC3, PANC-1, Ins1-E, M1CF-7, HaCat, Caco-2 cell lines	[53]
Buddleia	<i>Buddleja davidii</i> Buddlejaceae	China	AChE inhibitory activity	Linarin isolated from plant inhibit AChE activity	[54]
Cape honeysuckle	<i>Tecomaria capensis</i> Bignoniaceae	South Africa	Analgesic, antipyretic, anti-inflammatory activities	Methanolic extract of leaves significantly prevented increase in volume of paw edema	[55]
Cat's claw creeper	<i>Macfadyena unguis-cati</i> Bignoniaceae	Central and South America	Anti-inflammatory, cytotoxic	Crude ethanol extract exhibited marked anti-inflammatory and cytotoxicity against lung cancer cell line	[56]
Chocolate vine	<i>Akebia quinata</i> Lardizabalaceae	China, Korea, Japan	Anti-fatigue agent	Akebia extract showed marked improvement in lethargic behavioral test	[57]
Clematis	<i>Clematis flammula</i> Ranunculaceae	Southern Europe and Northern Africa	Cytotoxic	Weed extract cause kinases and transcription factor induction	[58]
Climbing spindle berry	<i>Celastrus orbiculatus</i> Celastraceae	Eastern Asia, Korea, Japan, China	Against gastric cancer	Compound 28-hydroxy-3-oxoolean-12-en-29-oic acid inhibited the migration and invasion of gastric cancer cells	[59]
Darwin's barberry	<i>Berberis darwinii</i> Berberidaceae	Chile, Argentina	Alzheimer's disease	Methanolic extract of stem bark exhibited acetylcholinesterase inhibitory activity	[60]
Elder	<i>Sambucus nigra</i> Caprifoliaceae	Europe, West Asia, North Africa	Antioxidant	Free radical scavenging potential	[61]
Elephant ear	<i>Alocasia brisbanensis</i> Araceae	Ceylon, Tahiti	Antimicrobial	Extract showed promising antimicrobial activities against <i>Staphylococcus aureus</i>	[62]
False acacia	<i>Robinia pseudoacacia</i> Fabaceae	South Eastern USA	Antitumor	Inhibition of IL-1β signaling	[63]
False tamarisk	<i>Myricaria germanica</i> Tamaricaceae	Eurasia	Cytotoxic	Compound tamgermanitin exhibited potent anti cancer effect	[64]
Field horsetail	<i>Equisetum arvense</i> Equisetaceae	Temperate Northern Hemisphere	Antioxidant	Potent antioxidant in DPPH assay	[65]
Green daphne laurel	<i>Daphne laureola</i> Thymelaeaceae	North Africa, South West Europe	Anticancer	Cytotoxic against lung cancer	[66]
Green goddess	<i>Zantedeschia aethiopica</i> Araceae	South Africa	Antimicrobial	Peptides in weed exhibited antimicrobial activities	[67]
Gypsywort	<i>Lycopus europaeus</i> Lamiaceae	Europe, Asia	Antimicrobial	Compound euroabienol showed broad spectrum activity	[68]

Hop	<i>Humulus lupulus</i> Cannabaceae	Europe, Western Asia, North America	Osteogenic	Activity evaluated via MC3T3-E1 cells lines	[69]
Horned poppy	<i>Glaucium flavum</i> Papaveraceae	Western Europe, South Western Asia	Against breast cancer	Bocconoline compound isolated from the plant inhibit viability of cancer cells	[70]
Houttuynia	<i>Houttuynia cordata</i> Saururaceae	Asia	Antiviral	Houttuynoid B isolated from the weed prevents cell entry of Zika virus	[71]
Ivy	<i>Hedera helix</i> Araliaceae	Europe, North Africa	Anti-inflammatory	Inhibition of <i>Staphylococcus aureus</i> strain	[72]
Jerusalem cherry	<i>Solanum pseudocapsicum</i> Solanaceae	South America	Acetylcholinesterase inhibitor	Alkaloids reported in the plant exhibited AChE inhibition	[73]
Lantana	<i>Lantana camara</i> Verbenaceae	Tropical America	Sedative	Essential oil from weed possess CNS depressant effects	[74]
Mexican water lily	<i>Nymphaea mexicana</i> Nymphaeaceae	Mexico	Anti-inflammatory	Cox-2 inhibition	[75]
Nasturtium	<i>Tropaeolum majus</i> Tropaeolaceae	Europe, America, Africa, Asia	Antimicrobial	Compound 3-[3-pyridinyl]-1,2,4-oxadiazol-5-yl] benzonitrile exhibited potent antimicrobial activities	[76]
Needlebush	<i>Hakea sericea</i> Proteaceae	Australia	Cytotoxic	Extract inhibited MCF-7 cell line	[77]
Old man's beard	<i>Clematis vitalba</i> Ranunculaceae	Europe, South West Asia	Antinociceptive and antipyretic	Vitalboside isolated from weed exerted action	[78]
Pig's ear	<i>Cotyledon orbiculata</i> Crassulaceae	Africa	Anticonvulsant	Aqueous and methanolic extracts showed prominent effects on gabaergic and glutaminergic mechanisms	[79]
Pink ragwort	<i>Senecio latifolius</i> Asteraceae	South Africa	Cytotoxic	Cytotoxicity in HepG2 cells caused depletion of cellular GSH	[80]
Rough horsetail	<i>Equisetum hyemale</i> Equisetaceae	Temperate Northern Hemisphere	Antitrypanosomal	n-butanol fraction exert antiprotozoal effect	[81]
Royal fern	<i>Osmunda regalis</i> Osmundaceae	Europe, India, Africa	Inhibition of head and neck cancer cell proliferation	Extract revealed growth inhibiting effect on HLaC78 and FaDu	[82]
Tree privet	<i>Ligustrum lucidum</i> Oleaceae	China	Hepatocellular carcinoma	Inactivation of PL3K/Akt pathway	[83]
Tutsan	<i>Hypericum androsaemum</i> Clusiaceae	South and Western Europe	Anti-lipid peroxidation	n-hexane fraction exerted desired activity	[84]
Chingma lantern	<i>Abutilon theophrasti</i> Malvaceae	Temperate region	Antibacterial	Extract showed activity against <i>Staphylococcus aureus</i>	[85]
Black night shade	<i>Solanum nigrum</i> Solanaceae	North Western Africa	Antitumor	Active against breast cancer cell line MCF7	[86]
Broad leaved dock	<i>Rumex obtusifolius</i> Polygonaceae	Eurasia	Hypoglycemic	Ethanol extract improved glucose tolerance in rabbits	[87]
Broad leaved fleabane	<i>Conyza sumatrensis</i> Asteraceae	South America	Antiplasmodial	Study confirmed the traditional use of weed	[88]
Broad leaved plantain	<i>Plantago major</i> Plantaginaceae	Eurasia	Potential wound healer	Showed activity against hyaluronidase and collagenase enzymes	[89]
Chick weed	<i>Stellaria media</i> Caryophyllaceae	India	Antifungal	Peptides in weed were responsible for its potent activity	[90]
Cleavers	<i>Galium aparine</i> Rubiaceae	Temperate zone	Immunomodulator	Ethanol extract stimulated immunocompetent blood cells	[91]
Dandelion	<i>Taraxacum officinale</i> Asteraceae	Africa	Antioxidant	Extract from leaf provide protection against free radical mediated oxidative stress	[92]
Father	<i>Chenopodium album</i> Amaranthaceae	Temperate zone	Antioxidant	Weed showed protection against mercury induced oxidative stress	[93]
Galinsoga	<i>Galinsoga parviflora</i> Asteraceae	Tropical America	Photocarcinogenesis	Caffeic acid derivative protect dermal UVA-induced oxidative stress	[94]
Hedge mustard	<i>Sisymbrium officinale</i> Brassicaceae	Southern Europe	Inhibition of oxidative mutagenicity	Polyphenols in weed exhibited desired action	[95]
Hemlock	<i>Conium maculatum</i> Apiaceae	Temperate region	Antimicrobial	Essential oils reported in weed showed activity against <i>Pseudomonas aeruginosa</i>	[96]
Manuka	<i>Leptospermum scoparium</i> Myrtaceae	New Zealand, South East Australia	Antibacterial	Oils exhibited activity against gram negative pathogens	[97]
Nettle	<i>Urtica urens</i> Urticaceae	Europe	Anxiolytic	Extract increased the time spent in bright-lit chamber of light/dark box pharmacological model	[98]
Pennyroyal	<i>Mentha pulegium</i> Lamiaceae	Northern Africa	Antidiabetic	Aqueous extract revealed improvement of glucose tolerance in in-vivo rat model	[99]
Red dead nettle	<i>Lamium purpureum</i> Lamiaceae	Eurasia	Haemostatic activity	Extracts showed promising results in haemostatic test	[100]
Scarlet pimpernel	<i>Anagallis arvensis</i> Primulaceae	Northern Africa	Molluscicidal	Aqueous leaf extract showed activity against <i>Schistosoma mansoni</i>	[101]
Scotch thistle	<i>Cirsium vulgare</i> Asteraceae	Europe	Hepatoprotective	Hexane extract showed anti-necrotic and anti-cholestatic effects	[102]
Scrambling speedwell	<i>Veronica persica</i> Plantaginaceae	Eurasia, America	Antiviral	Extract showed synergistic activity in combination with acyclovir anti-HSV therapy	[103]

Selfheal	<i>Prunella vulgaris</i> Lamiaceae	Eurasia, America	Inhibition of IHNV infection	Ursolic acid decrease cytopathic effect and viral titer	[104]
Sow thistle	<i>Sonchus oleraceus</i> Asteraceae	Asia	Nephroprotective	Extract showed desired effect by inhibiting ischemia reperfusion in rats	[105]
Water pepper	<i>Persicaria hydropiper</i> Polygonaceae	Eurasia	Anti-inflammatory	Extract showed desired therapeutic effect	[106]
Yarrow	<i>Achillea millefolium</i> Asteraceae	Eurasia, North America	Antibabesial activity	Different extract were active against <i>Brucella canis</i>	[107]
Woolly mullein	<i>Verbascum thapsus</i> Scrophulariaceae	Eurasia	Antimicrobial	Ethanollic extract were potent against gram positive bacteria	[108]
Wild teasel	<i>Dipsacus fullonum</i> Caprifoliaceae	Australia	Antibacterial	Compounds isolated from root exhibited activity against <i>Staphylococcus aureus</i>	[109]
Cocklebur	<i>Xanthium strumarium</i> Asteraceae	Temperate zone	Hepatocellular carcinoma	Weed induce apoptosis in HCC cell lines in a dose dependent manner	[110]

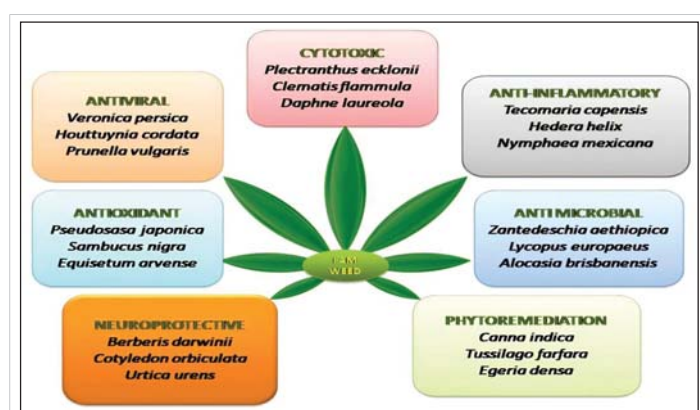


Figure 1: Therapeutic potential of weeds.

include *Clematis flammula* [58], *Hakea sericea* (Needlebush) [77], *Robinia pseudoacacia* (False acacia) [63], *Daphne laureola* [66], *Myricaria germanica* (False tamarisk) [64], *Senecio latifolius* (Pink ragwort) [80], *Osmunda regalis* (Royal fern) [82]. Parvifloron D isolated from *Plectranthus ecklonii* via flash dry column chromatography exhibited antiproliferative effects against pancreatic cancer when evaluated against HaCat, BxPC3, Caco-2, MCF-7, Ins1-E and PANC-1 cell lines [53]. Aqueous extract of weed *Solanum nigrum* at concentration of 10 g/l caused 43% cytotoxicity in MCF7 cell line by inhibiting migration, suppression of hexokinase and pyruvate kinase [86]. Triterpene (28-Hydroxy-3-oxoolean-12-en-29-oic acid) present in *Celastrus orbiculatus* showed inhibitory activity on SGC-7901 and BGC-823 cells lines [59]. Bocconoline alkaloid isolated from dried roots of *Glaucium flavum* (Horned poppy) exhibited cytotoxicity with  $IC_{50}$  value of  $7.8\mu M$  [70].

**Antimicrobial weeds:** Invasive weed *Aristea ecklonii* containing Plumbagin exhibited antimicrobial activity with minimum inhibitory concentration between  $2\mu g/ml$  and  $16\mu g/ml$  [50]. Antimicrobial peptides isolated from arum lily (*Zantedeschia aethiopica*) exhibited potent antimicrobial activity [67]. Euroabienol (abietane-type diterpenoid) isolated from fruits of *Lycopus europaeus* exhibited broad spectrum antimicrobial activity [68]. Compounds 3-[3-(3-pyridinyl)-1,2,4-oxadiazol-5-yl] benzonitrile and [3,5-Bis (1,1-dimethylethyl)-4-hydroxyphenyl] isolated from weed *Tropaeolum tuberosum* when tested against *Candida tropicalis* exhibited antifungal activities with MICs of  $100\mu M$

and  $50\mu M$  [76]. Extracts obtained from leaves of weed *Abutilon theophrasti* elicit antimicrobial potential against *Staphylococcus aureus*, *Salmonella*, *Streptococcus* and *E. coli* species [85]. Essential oils isolated from weeds *Conium maculatum*, *Leptospermum scoparium* showed antimicrobial activity against several strains of *Pseudomonas aeruginosa* [96,97]. Ethanollic extracts of woolly mullein reported positive against gram positive bacteria (*Bacillus cereus*) [108]. Phenolic compounds from *Dipsacus fullonum* exerted inhibitory effects on *Staphylococcus aureus* DSM 799 and *E. coli* ATCC 10536 strains [109].

**Antioxidant weeds:** Strong antioxidant activity was reported by ferulic acid derived from leaves of weed *Pseudosasa japonica* when evaluated using DPPH (54 %) and ABTS (65 %) [51]. Antioxidant potential of *Taraxacum officinale* was determined using *in vitro* methods (DPPH, ABTS, FRAP). The ABTS method revealed that antioxidant activity was  $156\pm 5.28\mu g/ml$  [92]. Other potential antioxidant weed includes *Acanthus mollis* [52], *Sambucus nigra* [61], *Equisetum arvense* [65].

**Anti-inflammatory weeds:** A study by Akhtar, et al. 2019 investigated the anti-inflammatory properties of *Hedera helix* and its major compounds on *Staphylococcus aureus* induced inflammation in mice. Hederacoside-C isolated from weed exerted profound anti-inflammatory effects [72]. Mexican water lily (*Nymphaea mexicana*) was found to be potent COX-2 inhibitor [75]. Active compounds isolated from aerial parts of weed *Clematis vitalba* when evaluated *in vivo* against carrageenan, serotonin, PGE-2 induced hind paw edema showed antinociceptive and antipyretic effects [78]. Methanolic extract of leaves of *Tecomaria capensis* significantly prevented increase in volume of paw edema [55]. Extract of *Persicaria hydropiper* exerted marked anti-inflammatory effects [106]. Aqueous extract alongwith compounds (calceorioside B, homoplantagin, plantamajoside) isolated from the aerial parts of *Plantago major* showed inhibition against hyaluronidase enzyme [89].

**Antiviral weeds:** Methanolic extract of scrambling speedwell weed (*Veronica persica*) reported potent activity against herpes simplex viruses and synergistic activity in combination with acyclovir anti-HSV therapy [103]. Ursolic

acid isolated from weed *Prunella vulgaris* inhibited IHNV infection in aquaculture with an inhibitory concentration of 99.3 % at 100 mg/l [104].

**Weeds acting on CNS:** Methanolic extract of stem bark of Darwin's barberry (*Berberis darwinii*) inhibited acetylcholinesterase *in vitro* with  $IC_{50}$  value of  $1.23 \pm 0.05$  microg/mL thereby provide relief in Alzheimer's disease [60]. Alkaloid solanocapsine isolated from weed *Solanum pseudocapsicum* reported to inhibit activity of enzyme acetylcholinesterase [73]. Nettle (*Urtica urens*) exhibited anxiolytic activity in mice when evaluated using hole board test, light-dark box test and rota rod test. Extract showed increased head-dip duration and head-dip counts in hole board test [98]. Aqueous (50-400 mg/kg i.p.) and methanolic extracts (100-400 mg/kg i.p.) of Pig's ear (*Cotyledon orbiculata*) exhibited anticonvulsant activity which predominantly delayed onset of seizures induced by N-methyl-DL-aspartic, bicuculline, picrotoxin in mice models [79].

**Other pharmacological activities of weeds:** Aqueous extract of *Akebia quinata* showed positive effect against fatigue in mice exposed to chronic restraint stress when evaluated using forced swimming behavioral test, sucrose preference and open field tests [57]. n-butanol fraction of weed *Equisetum hyemale* exerted antiprotozoal effects against *Trypanosoma evansi* trypanomastigotes after nine hours exposure [81]. Chen, et al. 2019 reported osteogenic activities of *Humulus lupulus* in MC3T3-E1 cell lines [69]. Ethanolic extract of weed *Galium aparine* stimulated the transformational activity of immunocompetent blood cells *in vitro* [91]. Aqueous extract of aerial parts of *Mentha pulegium* (20 mg/kg) showed antihyperglycemic effect by marked improvement in oral glucose tolerance test in streptozotocin induced diabetic rats [99]. Butanolic extracts of aerial parts of *Lamium album* and *Lamium purpureum* showed haemostatic activity in wistar rats when evaluated by tail bleeding time determination and acenocoumarol carrageenan test compared to vitamin K [100]. *Anagallis arvensis* (Scarlet pimpernel) leaf extract showed molluscicidal activity against *Biomphalaria alexandrina* at  $LC_{50}$  37.9 mg/l and  $LC_{90}$  48.3 mg/l [101]. Hexane extract rich in lupeol acetate of weed scotch thistle (*Cirsium vulgare*) prevented carbon tetrachloride induced liver damage in rats by diminishing lipid peroxidation and nitric oxide levels [102]. Extracts of *Sonchus oleraceus* (Sow thistle) were reported to be nephroprotective against kidney ischemia reperfusion injury in wistar rats [105]. Water extract, ethanol extract, hexane/acetone extract obtained from *Achillea millefolium* (Yarrow) were effective against *Babesia canis* parasite at 2 mg/ml concentration [107].

### Other potential applications of weeds established in New Zealand

A large number of weed communities has been reported to clean environment through phytoremediation process and act as bioindicators (Figure 2). Phytoremediation is

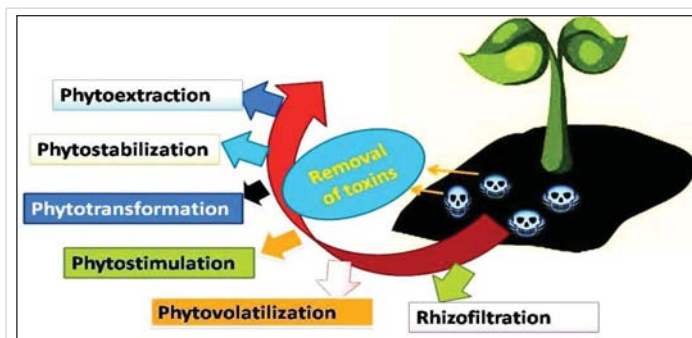


Figure 2: An overview of Phytoremediation process.

described as a process of eradicating toxic contaminants from soil, water and air. This process involves phytoextraction (harvesting of biomass), phytostabilization (contaminants stabilized into less toxic compounds), phytotransformation (chemical modification of contaminants), phytostimulation (rhizosphere degradation), phytovolatilization (conversion of toxic compounds into volatile form) and rhizofiltration (filtration through roots) [111]. Arum lily (*Zantedeschia aethiopica*) acts as micropollutant removal by removing accumulation of copper, zinc, carbamazepine and linear alkylbenzene sulphonates [112]. Bladderwort (*Utricularia gibba*) [113], canna lily (*Canna indica*) [114], coltsfoot (*Tussilago farfara*) [115], egeria (*Egeria densa*) [116], giant buttercup (*Ranunculus acris*) [117], broom (*Cytisus scoparius*) [118], annual poa (*Poa annua*) have been involved in removing toxic metals (chromium, cadmium, zinc, lead) from the environment [119]. Parrot feather (*Myriophyllum aquaticum*) aids in removing antibiotic (tetracycline) from water [120]. Oxeye daisy (*Leucanthemum vulgare*) potentiated crude oil phytoremediation and used in eliminating pollution from environment [121]. Apart from these properties weeds have also been found to be employed in other industries e.g. buffalo grass weed (*Stenotaphrum secundatum*) used in turf grass industry [122]. Mucoadhesive properties of water soluble gum obtained from *Hakea gibbosa* added in sustained release dosage forms [123]. Silver nanoparticles having average particle size 20 nm synthesized from *Cestrum nocturnum* showed more antioxidant potential as compared to vitamin C along with strong antibacterial activity against *Vibrio cholerae* with MIC of 16 µg/ml [124]. Organic fertilizer manufactured via aquatic weed *Salvinia molesta* when evaluated using FT-IR, plant bioassay test for determination of its fertilizer value and chemical composition showed promising results as vermicompost [125]. Eragrostis species (*E. capensis*, *E. curvula*) and grass *Stenotaphrum secundatum* exhibited drought resistant ability [126,127].

Besides the therapeutic potential exhibited by weeds, toxicity profile should be taken into consideration while exploring them. *Equisetum arvense* (Field horsetail) exerted hepatotoxicity in rats [128], weeds like *Zantedeschia aethiopica* (Arum lily), *Conium maculatum* (Hemlock), *Solanum nigrum* (Black night shade) are considered poisonous in New Zealand



Important abbreviations used		
ABTS	=	2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)
COX	=	Cyclooxygenase
DPPH	=	2,2-diphenyl-1-picrylhydrazyl
ESI	=	Electrospray ionization
FAB	=	Fast atom bombardment
FRAP	=	Fluorescence recovery after photobleaching
FTIR	=	Fourier-transform infrared spectroscopy
GC	=	Gas chromatography
GSH	=	Glutathione
HepG2	=	<i>Hepatoblastoma cells</i>
HPLC	=	High-performance <i>liquid chromatography</i>
HPTLC	=	High-performance thin-layer chromatography
HRESIFTMS	=	High resolution electrospray ionization fourier transform mass spectrometry
HR-ESI-MS	=	High-resolution electrospray ionization mass spectrometry
HSV	=	<i>Herpes simplex virus</i>
IC <sub>50</sub>	=	Inhibitory concentration
IHNV	=	Infectious hematopoietic necrosis virus
LC-ESIMS	=	Liquid chromatography electrospray ionisation mass spectrometry
MCF7, SGC-7901, BGC-823 cells, BxPC3, PANC-1, Ins1-E, MCF-7, HaCat, Caco-2, HCC, HLaC78, FaDu	=	Cancer cell lines
MS	=	Mass spectrometry
NMR	=	Nuclear magnetic resonance
NO	=	Nitric oxide
PGE-2	=	Prostaglandin E2
TLC	=	Thin layer chromatography
UAE	=	Ultrasound-assisted <i>extraction</i>
UV	=	Ultraviolet spectroscopy
UVA	=	Ultra violet radiation

[129]. *Hedera helix* (Ivy) caused contact dermatitis [130], *Lantana camara* exerted *in vivo* cell toxicity [131], *Xanthium strumarium* (Cocklebur) responsible for causing poisoning in cattle [132].

## Conclusion

Humans define weeds as per their appropriateness and understanding of the plant. A plant investigated as weed in some region may be a plant of medicinal importance for another region. The usefulness of weeds has been ignored by humans for long time because of their invasive growth, competitors of genuine crop and no economic value. This human behaviour might be developed over time due to lack of proper knowledge of phytochemical screening as well as therapeutic potential of weeds. Weeds are the sources of human food, fodder in agriculture, shelter for some animals, helpful against soil erosion, indicators of soil nutrients, as well as sources of commercially important essential oils. In this era weeds have been extensively explored for their immense phytopharmacological prospects. It is evidenced that weeds have been sources of potential targets for different pathological conditions. However there is need of more scientific and clinical investigations required in assessment of toxicity profile to get the maximum potential of weeds. Weeds have protective role in environment as a component of phytoremediation and for sustainable ecosystem. Because of immense therapeutic potential implicit by weeds a new chain of thoughts emerge in our mind to consider the value

of these important plants so called 'weeds'. Are they need to be redefined or we need to rethink the concept of weeds? It is clear from the studies documented in this review that the approach of whether a plant is wanted or not should depends on its pharmacological potential and role in ecosystem other than merely the competitive effect of plant with the particular crop. Further advancements are required in order to spin the concept of weeds into therapeutic weeds.

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