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Wedelia chinenis (Asteraceae) – An overview

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ABSTRACT

Objective: The plant *Wedelia chinensis* (*W. chinensis*) belonging to family Asteraceae (sunflower family) has great importance in Ayurvedic, Sidhha and Unani systems of traditional medicine. Thorough screening of literature available on *W. chinensis* depicted the fact that it is a popular remedy among the various ethnic groups, Ayurvedic and traditional practitioners for treatment of various ailments. Extensive studies show presence of flavonoids, diterpenes, triterpene saponins and phytosteroids. *W. chinensis* is reported to possess antioxidant, anti-inflammatory, analgesic, antimicrobial, hepatoprotective, CNS depressant, anti-osteoporic, anticonvulsant, wound healing, sedative, antistress, antiulcerogenic and anticancer activity. This work gives an overview of the phytochemical and pharmacological evidence of *W. chinensis*. Although more studies are necessary to explore the therapeutic potential of this plant as, it has more therapeutic properties which are not known.

1. Introduction

Drugs of natural origin play a significant role in the public health care system of any nation. Indian Materia Medica includes about 2 000 drugs of natural origin of which approximately 400 are mineral and animal origin while the rest are of vegetable origin Ayurveda, Siddha and Unani systems 600-700 herbs for medicinal use[1,53]. The World Health Organization (1980) has also recommended the evaluation of the effectiveness of plants in conditions where there is lack of safe synthetic drugs[2, 53].

Wedelia chinensis (*W. chinensis*) (Osbeck) Merill, Asteraceae is a reputed herbal medicine in Ayurvedic, Siddha and Unani system of medicine. It is a scabrous procumbent perennial soft herb with high camphor like odor and has a gorgeous growth[3,7]

2. Botanical description

A perennial herb 0.3-0.9 m high, stem procumbent at base and rooting at the lower nodes, terete, more or less appressedly hairy. Leaves are opposite, subsessile, 2.5-7.5 by 1-2.8 cm lanceolate-oblong, entire or irregularly crenate-serrate, scabrous with short white hairs or at length more or less glabrate, base tapering. Heads 2.0-3.2 cm diameter, solitary; peduncles 2.5-15.0 cm long erect, slender, slightly thickened beneath the heads (Figure 1)[4].

Figure 1. Flowering shoots of *W. chinensis*.

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3. Traditional use

The literature reveals that various parts of *W. chinensis* have been used as a folklore medicine for various ailments like its hepatoprotective efficiency, cholagouge, jaundice, diarrhea, couch, cephalahgia, diphtheria and pertusis *etc*[5].

The properties are the same as those of *Eclipta alba* (*E. alba*) (Ayurveda). In decoction the plant is used as a deosurbent and is given in uterine haemorrhage and menorrhagia. The leaves are considered tonic, alterative and useful in cough, cephalagia, skin diseases and alopecia. An infusion of the plant is given in Indo China for the swelling of the abdomen[4,6,7]. The decoction of the plant was extensively used by the tribes in Kolli Hills of Namakkal District, Tamilnadu, India, to reduce mental tension and also to induce sleep and the plant affects CNS[7].

The plant is astringent, bitter, acrid, thermogenic, anti-inflammatory, vulnery, ophthalmic, cardiotonic, anthelmintic , diuretic, aphrodisiac, sudorific, febrifuge and trichogenous and is useful in vitiated conditions of Kapha and Vata, inflammation, elephhanmtiasis, otalgia, cephalagia, wounds, ulcers, nyctalopia, dysopia, hepatosplenomagaly, colic, dyapepsia, helminthiasis, strangury, anaemia. Sminal weakness, fever, baldness and graying of hair. The *W. chinensis* plant is very specific for 'viral hepatitis' [8,9]. Traditionally the fruits, leaves and stem are used in childbirth and in the treatment of bites and stings, fever and infection. The leaves are used in the treatment of kidney dysfunction, cold, wounds and amenorrhea[10]. *W. chinensis* is a very useful herbal medicinal plant. Its leaves can be used in treatment of dermatological disorders, cough, headache, hair loss, lice, strengthening the nervous system, lack of blood, digestive system disorders. The leaves are used in dyeing grey hair and in promoting the growth of hair. They are considered tonic, alternative, and useful in coughs, cephalalgia, skin diseases, and alopecia. The juice of the leaves is much used as a snuff in cephalalgia. The seeds and flowers, as well as the leaves, are used in decoction, in the quantity of half of teacupful twice daily, as deobstruent. In decoction, the plant is used in uterine haemorrhage and menorrhagia. *W. chinensis* using home remedy Osteochondritis dissecans, Multiple sclerosis, Juvenile arthritis, Gouty arthritis, Rheumatic fever, etc. leaves extracts are a natural alternative to commonly used anti-inflammatory drugs like Dolonex (Piroxicam), Brufen (Ibuprofen) and Voveran etc. *W. chinensis* leaves extract can be used with confidence for treating Rheumatic fever[11].

4. Habitat and synonyms

W. chinensis is a procumbent, perennial herb found in wet places in Uttar Pradesh, Assam, Arunachal Pradesh and all along the coastal areas[12]. Bengal, Burma, Konkan, plains districts of Madras Presidency, Ceylon- Malay Archipelago, China and Japan[4].

Parts used: Leaves, Stem, Whole plant.

The 'Bhringraj' has been included in the category 'Dasapuspam' in Ayurveda. Four plants viz *Wedelia calendulaceae* (*W. calendulaceae*), *E. alba*, *Heliotropium strigosum* (*H. strigosum*) and *Viscum album* (*V. album*) are known by the name Bhringaraj[13]. Bengal: Bangra, Bombay: Pivalabhangra-; Chinese: Pang K'iKiou-; Hindi: Bhangra, Bhanra-; Sanskrit: Bhringaraja, Pitabhringaraja; Tamil: Manjalkarilamkanni[4,14].

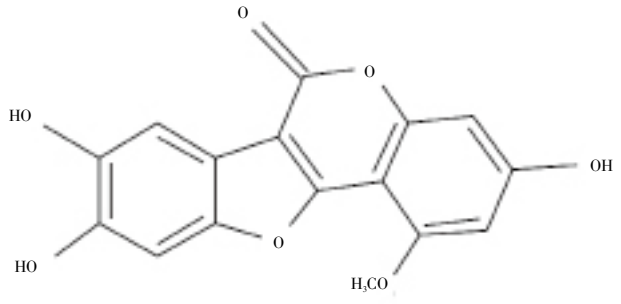
5. Phytochemistry

Extensive studies have been carried out on *W. chinensis*. Chemical components isolated from the plant are as follows: The expressed juice of the herb contained an oil-soluble black dye, 11.2; tannin, 220; carotene, 1.14; Chlorophyll, 3.75; Saponin (contradictory report), 500; phytosterol, 3.75; waxy compound, 29.7; resin, 44; chloroform extract(resinous mass), 27; gum, 80; total sugar, 1 040 mg/100 g juice. An Indian analysis of the herb gave negative test for alkaloid, but the Chinese investigations showed the presence of an alkaloid in the stems, leaves and flowers. The leaves contain isoflavanoids and wedelolactone (I) (0.05%). The latter is the lactone of 5:6-dihydroxy-2-(2:6-dihydroxy-4-methoxyphenyl) benzofuron-3-corboxylic acid and analogous in structure to coumestrol an estrogen from clover[5,15-17,22].

The leaves contain isoflavonoids, bisdesmosidic oleanolic acid saponins and wedelolactones[18,19,22,43]. Norwedelolactone (II) has also been isolated from alcoholic extract of leaves[20,22].Norwedelic acid (III) (5, 6-dihydroxy-2 (2′, 4′, 6′-trihydroxyphenyl)-benzofuran-3-carboxylic acid) [18,22].

Triterpenoid saponin: bisdesmodic- osidic oleanolic acid saponins have been isolated from fresh leaves of this plant, of the three saponins one is a new bisdesmisidic oleanolic acid saponin, which has been identified as β-D-glucopyranosyl-3-o-[o-β-D-xylopyranosyl-(1 H, 2)-β-D-Glucuronopyranosyl] oleanolate (IV), β-D-glucopyranosyl 3 β-[(o-β-D-xylopyranosyl-(1 H,)-(p-D-glucuronopyranosyl)]-olean-12-en-28 oate) (V) [21,22].

The active fraction of the methanolic extract of the herb contained fatty acids, melissic and lignoceric acid, stigmasterol and stigmasteryl glucoside, Kauren diterpenes-(-) kaur-16-en-19-oic acid(VI) and a mixture of the three esters, 3 α-angeloyloxy- (VII), 3 α-triglinoyloxy- (VIII) and 3 α-senecioyloxy-kaur-16-en-19-oic acid[23,43].

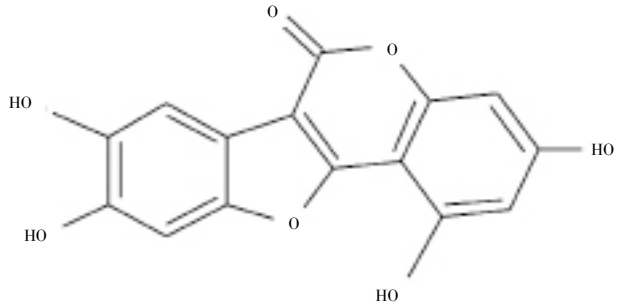


(I)Wedeloloactone

Figure 2. Structure of wedeloloactone.

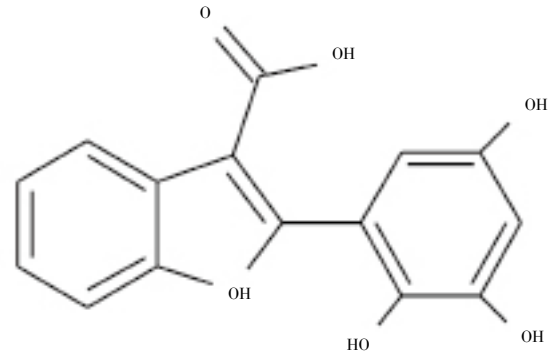
The herb is said to possess properties and main active constituents (coumestans *i.e.*, wedelolactone and de-methylwedelolactone) similar to Eclipta alba Hassk[24,25].

The essential oil of the aerial parts of the *W. chinensis* Merrill was analyzed by GC and GC/MS. Nineteen compounds have been identified accounting for 94% of the oil. It was made up of mainly monoterpenes hydrocarbons (50.6%), sesquiterpenes hydrocarbons (22.5%), oxygenated sesquiterpenes (20.3%) with only small amounts of oxygenated monoterpenes (0.7%). The main constituents were found to be α-pinene (21.7%), spathulenol (20.3%) and limonene (14.3%)[26]. Luteolin, apigenin, wedelolactone and indole-3-carboxyaldehyde were also reported[27].



(II) Norwdelolactone

Figure 3. Structure of norwdelolactone.



(III) Norwedelic acic

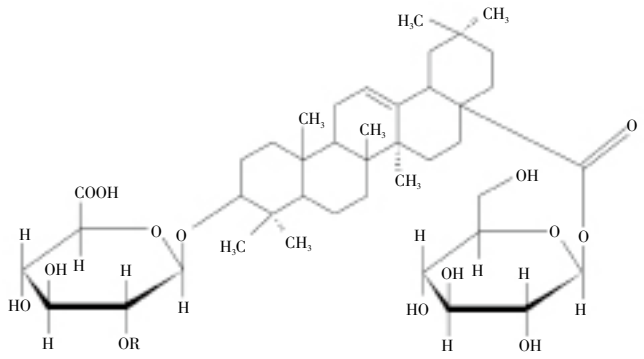
Figure 4. Structure of norwedeleic acid.

6. Pharmacological studies

Although a lot of pharmacological investigations have been carried out based on the ingredients present but a lot more can still be explored, exploited and utilized. A summary of the findings of these is presented below.

6.1. Hepatoprotective

The alcoholic extract of whole plant *W. calendulacea* exhibited protective activity against carbon tetrachloride-induced liver injury *in vivo*. The extract also increased the bile flow in rats suggesting stimulation of liver secretory capacity[12, 43].

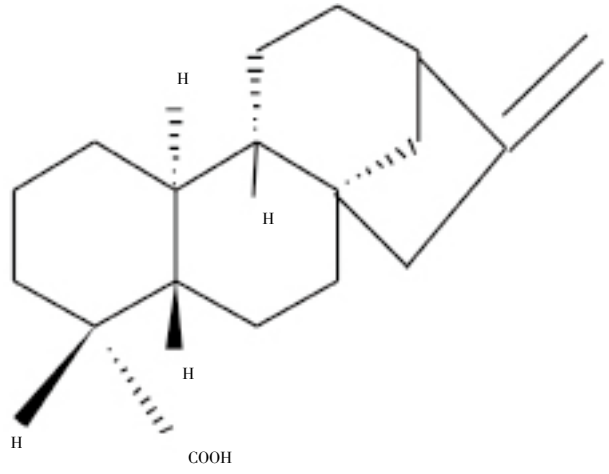


Tritcrpenoid saponin

(IV)R=b-D-xylopyranosyl

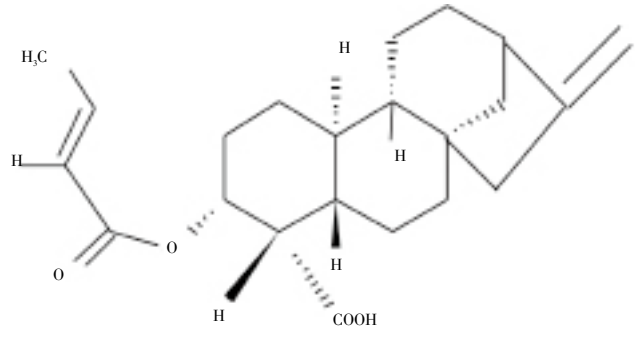
(V)R=b-D-glucopyranosyl

Figure 5. Structure of triterpenoid asponin.



(VI)(-)-kaur-16-en-19-oicacid

Figure 6. Structure of (-)-kaur-16-en-19-oic acid.

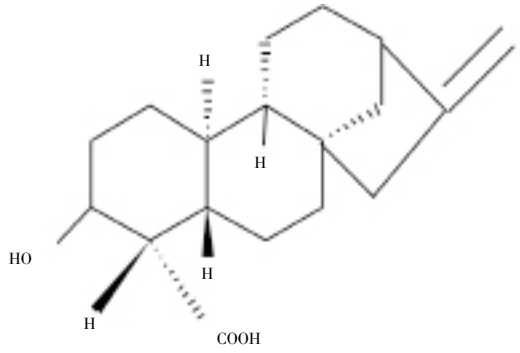


(VII)3a trigloyloxy kaur-16-en-oic acid

Figure 7. Structure of 3 α -trigloyloxy kaur-16-en-oic acid.

The hepatoprotective effects of a Taiwanese crude herb, Hwang-hua-mih-tsay (*W. chinensis* (Osbeck) Merr.), were reported. These serological observations were confirmed by histopathological examinations. A microscopic

examination of the liver showed a marked improvement in groups receiving *W. chinensis*. It further confirms the hepatoprotective effect of *W. chinensis*, all pharmacological and histopathological effects were compared with *Bupleurum chinense* DC. (Family Umbelliferae), a well documented antihepatotoxicity herb. It was concluded that *W. chinensis* has a definite hepatoprotective effect against liver injuries[28]. The ethyl acetate-soluble fraction of the drug *W. chinensis* exhibited antihepatotoxic activity in assays employing CCl_4-, GalN-, and phalloidin-cytotoxicity in rat hepatocytes. It showed a significant stimulatory effect on liver cell regeneration[24]. The coumestans showed the hepatoprotective effect against paracetamol induced hepatic injury[29]. The extracts of this plant have been tested in experimental animal models for their hepatoprotective effects[30]. The hepatoprotective activity of ethanolic extract of *W. calendulacea* was studied against CCl_4 induced acute hepatotoxicity in rats. The treatment with ethanolic extract of *W. chinensis* showed a dose-dependent reduction of CCl_4 induced elevated serum levels of enzyme activities with parallel increase in total protein and bilirubin, indicating the extract preserves the normal functional status of the liver[31]. The hepatoprotective effect of alcoholic and aqueous extract of whole plant of *W. chinensis* was found to possess significant protective effect against hepatotoxicity induced by CCl_4[32]. Antihepatotoxic activity of different extracts (petroleum ether, chloroform and methanol) of aerial parts of *W. chinensis* have shown significant activity by reducing the elevated levels of serum enzymes[33].

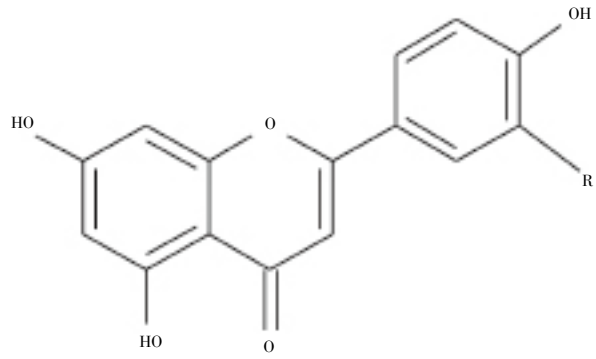


(VIII)3a- angeloyoxy kaur-16-en-oic acid

Figure 8. Structure of 3 α -angeloyloxy kaur--16-en-oic acid.

6.2. Wound healing

The effect of an aqueous extract of the leaves of *W. calendulacea* Less. on wound healing, in open and sutured wound models, was observed and found to be significant[32,35]. The wound healing efficacy of ethanolic leaf extract of *W. chinensis* was evaluated in excision, incision and dead space wound models. Its ethanolic extract was found to possess significant wound healing activity, which was evidenced by decrease in the period of epithelialization, increase in the rate of wound contraction, skin breaking strength, granulation tissue dry weight, and its breaking strength[36]. The effect of an aqueous extract of the leaves of *W. calendulaceae* on wound healing, in open and sutured models was observed and found to be significant[37].



(IX) R=H Apigenin
R= OH Luteolin

Figure 9. Structure of apigenim & luteolin.

6.3. Anticancer

The methanolic extract of *W. calendulaceae* (MEWC) was evaluated for its anticancer activity against Ehrlich Ascites Carcinoma (EAC) in Swiss albino mice. On day 1, the extract of *W. calendulaceae* at a dose of 250 and 500 mg/kg body weight was administered orally and continued for 9 consecutive days. The anticancer activity of MEWC was examined by determining the tumor volume, tumor cell count, viable tumor cell count, nonviable tumor cell count, mean survival time and increase in life span in experimental animal models. The extract increased the life span of EAC treated mice and restored the hematological parameters as compared with the EAC bearing mice. Thus, the study revealed that the MEWC showed anticancer activity in the tested animal models[38].

6.4. Immunostimulant

Immuno-stimulatory activity of *W. chinensis* has been reported[18,35].

6.5. CNS depressant

W. chinensis is found to affect the central nervous system[52]. The stem extract of *W. calendulaceae* possess a potent CNS-depressant action, mostly similar to that of psychopharmacological agents[35]. The ethanolic extract of whole plant of *W. chinensis* was investigated by common psychopharmacological tests. The reduction in exploratory behavior in animals was similar with the action of other CNS depressant agents. A significant lack in motor co-ordination and muscle relaxant activity was also noted in animals treated with crude extract. The results altogether indicates that the extract has CNS depressant activity[39].

6.6. Antioxidant

Based upon the results from different in vitro antioxidants model it is evident that Methanolic extract of *W.*

calendulaceae has an effective and considerable antioxidant profile[40].

6.7. Adaptogenic and antistress

The effect of alcoholic extract of *W. chinensis* leaves were evaluated on stress induced changes in brain neurotransmitters and enzyme monoamine oxidase levels in albino rats. The extracts were found to possess normalizing activity against cold immobilization stress induced changes in norepinephrine (NE), dopamine (DA), 5-hydroxy tryptamine (5-HT), 5-hydroxy indole acetic acid (5-HIAA) and enzyme monoamine oxidase (MAO). The results obtained provide biochemical evidence for antistress activity of the tested extracts[41].

6.8. Sedative

The neuropharmacological activities of the methanolic and aqueous extract of *W. calendulacea* stem were screened in rats and mice. The extracts effect on pentobarbital- induced sleeping time, pentylenetetrazole-and styrychnine- induced seizure, spontaneous motor activity, exploratory behavior and rota-rod performance (motor coordination) were evaluated. The methanolic extract (20 and 50 mg/kg, i.p.) and aqueous extract (200 and 500 mg/kg, i.p.) produced a significant (P<0.001) prolongation of pentobarbital-induced sleeping time, and reduced the SMA and exploratory behaviour. The extract prolonged onset of the phases of seizure activity but did not protect mice against lethality induced by pentylenetetrazole and strychnine. It also failed to affect the motor coordination test. These results suggest that the extract contained an agent with neuropharmacological activity that may be sedative in nature[35].

6.9. Anti-osteoporotic (post menopausal)

The anti osteoporotic effect of the ethanol extract of *W. calendulacea* in the ovariectomized rat model of osteoporosis at two different dose levels of 500 and 750 mg/kg body wt was studied. The findings, assessed on the basis of biomechanical and biochemical parameters, showed that the ethanol extract of the plant had a definite protective effect. This was further supported by the histopathological studies[42].

6.10. Chemopreventive

The chemopreventive effect of methanol extract of *W. calendulaceae* (MEWC) against 20-methylcholanthrene (20-MC) induced carcinogenesis in Swiss albino mice was studied. MEWC was administered orally at 250 and 500 mg/kg body weight for 90 consecutive days after 24 h of single subcutaneous administration of 20-MC (200 g) in mice and observed for 15 weeks to record tumor incidence (fibrosarcoma) and survival. After 15 weeks the mice were sacrificed for the estimation of hematological profiles and liver biochemical parameters *viz*. lipid peroxidation, reduced glutathione (GSH), glutathione-S-transferase (GST), superoxide dismutase (SOD) and catalase (CAT). MEWC treatment markedly reduced tumor incidence and prolonged life span of sarcoma bearing mice as compared to 20-MC control. Haematological profiles were significantly (P < 0.001) restored to normal levels in MEWC treated mice. MEWC treatment significantly (P < 0.001) modulated the aforesaid liver biochemical parameters as compared to 20-MC control. Therefore, *W. calendulaceae* possess remarkable chemopreventive efficacy in Swiss mice[43].

6.11. Analgesic and anti-inflammatory

Wedelolactones from *W. calendulaceae* was found to possess 5-lipoxygenase and caspase inhibitory activities[24,44]

The ethanolic extract of *W. chinensis* (EEWC) belonging to the family of Asteraceae was evaluated by hot plate and acetic acid induced writhing methods to assess its analgesic activity. The extract was also evaluated for its anti-inflammatory action by using on carrageenan, mediators such as histamine and serotonin induced paw oedema, and cotton pellet induced granuloma tests for its effect on acute and chronic phase inflammation models in rats, as well as analgesic activity in mice. It was found that the extract caused an inhibition on the writhing response induced by acetic acid in a dose dependent manner. Dose of 500 mg/kg EEWC and aspirin could block the writhing response by 51.92% and 68.68% (P<0.001), respectively. It was also indicated that the EEWC showed significant antinociceptive action in hot plate reaction time method in mice. This effect was comparable to that of standard drug morphine treated controls, suggesting the central activity of EEWC. Maximum inhibition (56.14%) was obtained at the dose of 500 mg/kg after 3 h of drug treatment in carrageenan induced paw oedema, whereas indomethacin (standard drug) produced 61.65% of inhibition. In the chronic model (cotton pellet induced granuloma) the EEWC (125, 250 and 500 mg/kg) and standard drug showed decreased formation of granuloma tissue by 56.69%, 34.57%, 43.30% and 55.23% respectively. The results indicate the potent analgesic and anti-inflammatory effects and therapeutic efficacy of *W. chinensis* extract on animal models which are comparable with those of standard drugs such as Aspirin, Morphine and Indomethacin respectively[45].

6.12. Androgen suppressing activity

Chronic inflammation can augment tumor development in various types of cancers, including prostate cancer (PCa). Reduction of inflammation is therefore an important anticancer therapeutic opportunity. Four anti-proliferative phytocompounds in *W. chinensis*, an oriental herbal medicine, identified through their ability to modulate the androgen receptor (AR) activation of transcription from prostate-specific antigen promoter in PCa cells. The 50% inhibition concentration values of indole-3-carboxylaldehyde, wedelolactone, luteolin and apigenin, were 34.9, 0.2, 2.4 and 9.8 mM, respectively. A formula that combined the phytocompounds in the same proportions as in the herbal extract decreased the dosage of each compound

required to achieve maximal AR inhibition. In correlation with the AR suppression effect, these active compounds specifically inhibited the growth of AR-dependent PCa cells and as a combination formula they also synergistically suppressed growth in AR-dependent PCa cells. The study identified the synergistic effects of active compounds in *W. chinensis* and demonstrated their potential in PCa prevention and therapy. The paradigm of multiple activities and synergism is a useful framework to investigate the therapeutic effects of whole extracts from assorted medicinal plant species[27].

6.13. Anthelmintic and febrifuge anticonvulsant

W. chinensis has been used as anthelmentic and febrifuge. The anticonvulsant activity of ethanolic and aqueous extract of whole plant of *W. chinensis* at a dose level of 250, 500, 750 mg/kg b.w, p.o. was performed in mice by using MES and PTZ methods. It was concluded that *Wedelia chinensis* extracts may have potential anticonvulsant activity[46].

6.14. Anti ulcerogenic and mucosal protective agent

The gastric antiulcer and ulcer healing effect of the ethanolic and aqueous extracts of the dried leaves of *W. calendulaceae* Less was found to be significant. The effect of the aqueous extract was observed to be more pronounced in comparison with that of the ethanolic extract[47]. A patent was filed for mucosal protective activity of *W. chinensis*[48]

6.15. Antibacterial & antimicrobial

The cytotoxicity and antibacterial activity of petroleum ether, chloroform and methanol extracts of *W. calendulaceae* were assayed by brine shrimp lethality bioassay and standardization disk diffusion method against 19 bacterial strains at a dose of 500 μg/disc. The crude petroleum ether, chloroform and methanol extract showed antibacterial activity[22,49]. The methanol extract of *W. chinensis* showed antibacterial activity against test organisms with the zones of inhibition ranging from 8-17 mm and the acetone extract shows the zone ranging from 8-13 mm[50].

6.16. Insecticidal

The alcoholic extracts of *W. chinensis* gave very good results to protect the plant against Plutella xylostella. All the experiments show the important role of the repellent effect on the pests. The ethyl acetate extracts of *W. calendulaceae* showed significant insecticidal activity against pests[22,51]

7. Conclusion

The above collected information regarding *W. chinensis* matches with the available literature. Natural products from folk remedies have contributed significantly in the discovery of modern drugs and can be an alternative source for the discovery of novel structures with better safety and efficacy profiles. Ethno-botanical and traditional uses of natural compounds, especially of plant origin received much attention in recent years as they are well tested for their efficacy and generally believed to be safe for human use. It is best classical approach in the search of new molecules for management of various diseases. Thorough screening of literature available on *W. cinensis* depicted the fact that it is a popular remedy among the various ethnic groups, Ayurvedic and traditional practitioners for treatment of various ailments. Researchers are exploring the therapeutic potential of this plant as it has more therapeutic properties which are not known.

Conflict of interest statement

We declare that we have no conflict of interest.

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