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**Mandal Bitasta**

Amity Institute of Pharmacy,  
Amity University, Noida  
(U.P), India.

**Dr. Swati Madan**

Amity Institute of Pharmacy,  
Amity University, Noida  
(U.P), India.

## *Aerva lanata*: A blessing of Mother Nature

**Mandal Bitasta, Dr. Swati Madan**

**Abstract**

*Aerva lanata* (Linn.) Juss. ex Schult. belonging to the family Amaranthaceae is a prostrate or succulent, perennial undershrub that grows on mountain slopes at a height of 900 metres from sea level. It is ordinarily called as Gorakhabooti in Hindi or Mountain knotgrass in English and is an asset bestowed by nature due to its numerous remedial qualities. It belongs to the Pashanbheda group of plants used to cure urinary stones. It possesses a wide variety of healing applications in traditional and folklore medicine in various geographical locations. It comprises of an extensive range of phytochemicals such as canthin-6-one and  $\beta$ -carboline alkaloids, flavonoids, phenolic acids, steroids, terpenoids and numerous other classes of phytoconstituents that contribute to its wide coverage of pharmacological activities. It bears antiurolithiatic, diuretic, hepatoprotective, anticancer, immunomodulatory, antioxidant, antimicrobial, and numerous other pharmacological activities thus making it a treasure of nature. The present review is an endeavour to provide a deep insight into the description, ethnomedicinal applications, pharmacognostic features, phytoconstituents, pharmacological and tissue culture studies explored till date.

**Keywords:** *Aerva lanata* (Linn.) Juss. ex Schult., Gorakhabooti, Pashanbheda, canthin-6-one alkaloids, antiurolithiatic

**Introduction**

Nature has been a vast reservoir of remedies in the form of medicinal herbs for the treatment of numerous ailments since ancient times. Plants have been a part of the therapeutic practice both in traditional and modern era. Herbs contain many phytoconstituents that contribute to their vast array of pharmacological activities leading to the production of beneficial effects. 80% of people throughout the world depend on herbal medicines for some fraction of their primary health care according to latest reports by World Health Organization [1]. Herbal medicines have gained popularity over conventional medicines owing to their reduced risk of side effects, effectiveness with chronic conditions, lower cost and widespread availability.

*Aerva lanata* (Linn.) Juss. ex Schult. is one such boon amongst the diverse medicinal herbs bestowed by nature. It is an erect, prostrate undershrub belonging to Amaranthaceae family [2]. It is called as Gorakshaganja, Satkabhedhi, Aadaanpaak in Sanskrit, Kapurijadi or Gorakhabooti in Hindi and Mountain knot grass in English [3]. It can be considered as Pashanbheda which, according to Ayurveda, is used to dissolve the stones in the urinary tract. It is grown 30-80 cm in height and is indigenous to tropical India, Tropical Africa, Saudi Arabia, Sri Lanka, Philippines, Java [4]. The plant finds an extensive range of traditional and folklore uses in different geographical locations. The whole plant is used by the local people of West Bengal [5] and the leaf decoction is used by the Nadars of Atoor village of Kanyakumari district to treat diabetes [6]. The decoction prepared from fresh leaves is administered orally by the people in tribal villages of Theni district in Tamil Nadu in case of inflammation due to kidney stones [7]. The whole plant and roots are used by tribal community of Odisha in the treatment of cholera [8]. The paste prepared from the whole plant is used for the cure of spermatorrhoea and the leaf paste is used for healing of wounds by the tribals of Niyamgiri hill area of Kalahandi district, Odisha [9]. The formulation of *Aerva lanata* combined with other herbs is used in the treatment of osteoporosis by the Sardar traditional medicinal practitioners of Bangladesh [10]. The Rai tribal practitioners of Rajshahi district of Bangladesh use the crushed roots of the plant with a little salt to treat leukorrhoea [11]. The plant finds use as astringent, diuretic, emollient, vermifuge, diuretic and in diabetes in the Vattamalai hills of Namakkal district of Tamil Nadu [12]. It is used to cure malarial fever, piles, hemorrhage and as an antidote for snake poison by Nadars and Kanis of

**Correspondence****Dr. Swati Madan**

Amity Institute of Pharmacy,  
Amity University, Noida  
(U.P), India.

Kanyakumari district, Tamil Nadu [13]. It is used in the treatment of kidney stones in the Aravali regions of Rajasthan [14]. The extract prepared from the roots is given in the cure of jaundice in sub-Himalayan regions of Uttarakhand [15]. The whole plant is used in asthma and chest pain by the Kani tribals in Tirunelveli hills of Western Ghats [16]. The villagers in Udhampur district of Jammu and Kashmir use the decoction prepared from the whole plant as a diuretic [17]. The leaves of the plant are used in the treatment of cough, fever, diabetes and hypertension in Andaman and Nicobar islands [18]. The whole plant and roots are used as astringent, suppurative, lithotriptic and cough by the villagers of Dindigul district, Tamil Nadu [19]. The roots are given in liver congestion, jaundice, biliousness, dyspepsia and the whole plant is used to treat pneumonia, typhoid and prolonged fevers in Eastern parts of Rajasthan [20]. The plant is employed as an anthelmintic and diuretic and the roots are used to cure headache in Krishna district of Andhra Pradesh [21]. The people in Chittoor district of Andhra Pradesh use the whole plant of *Aerva lanata* in the treatment of leucorrhoea, nephrocalcinosis and ureteral stones [22]. The root bark is given orally in the treatment of hydrocele in Odisha [23]. The fruit powder is used to treat pyorrhoea in Rayalaseema region of Andhra Pradesh [24]. The fruits are used as appetizer, in dysentery and heart tonic and the roots are used as demulcent and diuretic in the state of Rajasthan [25]. The whole plant is used in the treatment of skin ailments by the various tribals of Rajasthan [26].

### Botanical Description

**Morphology-** It is an erect or prostrate dioecious herb which grows upto 80 cm in height with cylindrical and branched tap root with a length of 7-2 cm and thickness of 2-8 mm with numerous fibrous lateral roots possessing a camphoraceous odour, yellowish brown from outer side and whitish from inner side [3]. It is branched at the base with the branches being pubescent or woolly- tomentose, striate [2]. Shoots are covered with smooth hairs [27]. Leaves are simple and alternate with lamina being elliptic or obovate or sub orbicular, along with obtuse or acute apex and tapering base and have white cottony hairs underneath [3]. The inflorescence consists of axillary heads or spikes [28]. Flowers are bisexual, small, sessile, greenish white with spikes [1]. Perianth is 1.5-1.25 mm in length and petals are silky-hairy on the back, oblong and obtuse and the fruit is ovoid in shape with shining black and kidney bean like seed [28].

**Microscopy-** The leaves consist of anomocytic stomata with the epidermal cells being smooth and curved and a vein termination number of 6-7. It shows the presence of multicellular uniseriate warty trichomes, rosette type calcium oxalate crystals (sphaeraphides), starch grains and rhomboidal crystals of calcium oxalate as evidenced from the powder study of the plant [29]. The leaf shows the presence of isodiametric cells in the upper and lower epidermis, rectilinear cell walls, conic multicellular hairs in the indumentum, unsubmerged stomata of anomocytic and hemiparasitic nature, dorsoventral mesophyll, palisade cells, spongy parenchyma with chlorophyll, conducting bundles and 8-10 radial chains of vessels [30]. Uniseriate trichomes having spinulated surface, multiarticulate and tapering at the end are also found in the leaves [27]. The transverse section of the roots contain 5-7 rows of cork cells with secondary cortex showing the presence of thin walled parenchymatous cells containing rosette crystals of calcium oxalate, 3-4

alternating rings of secondary xylem and phloem with pitted vessels, circular pith cells with rosette crystals of calcium oxalate [28]. Powdered roots show the presence of lignified and non-lignified cylindrical fibers, lignified xylem vessels having bordered pits, calcium oxalate crystals, simple, oval or rounded starch grains, tricho sclereid, cork cells, parenchyma cells and secondary phloem [31]. The stem shows the presence of thick-walled and small-celled epidermis, thick-walled collenchyma cells below the epidermis, cortex consisting of parenchyma, groups of pericyclic fibres, primary xylem vessels, radial chains of secondary xylem vessels, resin ducts, small rounded cells in the medulla [30].

### Phytoconstituents

*Aerva lanata* is loaded with a diverse range of phytoconstituents. Phytochemical screening showed the presence of numerous classes of phytochemicals such as alkaloids, steroids, flavonoids, tannins, amino acids and proteins, carbohydrates, cardiac glycosides, saponins and terpenoids [32]. The four different flavonols identified were quercetin, kaempferol, 4'-methoxy kaempferol and 4', 7-dimethoxy kaempferol. It also revealed the presence of phenolic acids such as vanillic acid, syringic acid, *p*-hydroxy benzoic acid, *p*-coumaric acid, ferulic acid and melilotic acid and the betacyanin named betanin was also identified [29]. Isorhamnetin-3-O- $\beta$ -D-glucoside and narcissin were isolated from the ground and air-dried material [33]. The FTIR analysis of the roots, stems, leaves and flowers showed the presence of various functional groups such as amide, alcohols, aldehydes, carboxylic acids, nitro compounds, ethers, amines, phenols, alkyl halides, ethers, etc. thus indicating the diversity of the chemical constituents in it [34]. It also contains phytoecdysteroids [35] and water-soluble polysaccharides, an acid polysaccharide, starch and hemi-celluloses were isolated from the leaves and flower heads [36]. The leaves are a reservoir of minerals such as K, Na, Ca, Mg, Zn, Fe, Mn [37]. Canthin-6-one alkaloids such as canthin-6-one, aervine, methergine, aervoside and  $\beta$ -carboline alkaloids such as 3- $\beta$ -carbolin-1-yl-propionic acid, aervolanine have also been isolated from the herb [38]. Other alkaloids isolated are canthin-6-one alkaloids such as ervine, methylervine, ervoside and  $\beta$ -carboline alkaloid ervolanine [39].  $\beta$ -sitosterol, daucosterol, feruloyltyramine, feruloyl vanillylamine have been found in the plant [40]. The whole plant also contains essential trace elements such as calcium, silicon, magnesium, potassium, chloride, carbon, oxygen [41]. The roots possess good amount of gallic acid as shown in ethanolic extract by HPTLC analysis [42]. Phytochemical screening of the roots extract also revealed the presence of quinones, phenols, triterpenoids, phytosterols and phlobatannins [43]. Aqueous extract of the stem showed the presence of 3,4,5-OH (gallic acid), apigenin-7-O-glucoside (apigetrin), quercetin-3-O-rutinoside (rutin) and 3,5,7,3,4,5-OH (myricetin) when analysed by HPLC [44]. The white and yellow coloured variants of *Aerva lanata* were found to contain methoxy kaempferol, total chlorophyll content, chlorophyll a and chlorophyll b [45]. The GC-MS analysis of leaves, stems, roots, flowers and seeds displayed a plethora of compounds such as pyridine, hydroquinone monobenzyl ether, docosane, dotriacontane, (R,Z)-12-hydroxy-9-octadecenoic acid, 2-isopropyl-2,5-dihydrofuran and a vast range of other compounds [46].

## Pharmacological Activities

### ➤ Antiurolithiatic activity

The aqueous extract of the aerial parts at a dose of 500 and 1000 mg/kg body weight decreased the urinary and kidney levels of stone promoting factors in ethylene glycol (0.75%) induced urolithic male albino Wistar rats, that is, calcium, oxalate and phosphate. Simultaneously, there was also a reduction in the levels of serum BUN, creatinine and uric acid [47]. The aqueous extract of the flowers showed a significant anti urolithiatic activity when subjected to *in vitro* and *in vivo* studies as evidenced from the loss of crystalline nature of the calcium oxalate crystals, reduction in the amounts of urinary stone forming constituents and improvement in the levels of nitrogenous substances to normal at a dose of 3.2 mg/kg body weight [48]. A polyherbal formulation of *Aerva lanata* with other herbs at a dose of 100 and 200 mg/kg decreased the levels of calcium and phosphate in the urine, serum uric acid, creatinine, urea and BUN in ethylene glycol (0.75%) induced urolithic rats. It also enhanced the urine pH, volume and magnesium content. The anti-urolithic activity was further evidenced by a decrease in the deposition of crystals in the kidney sections, tubular dilatation and necrosis [49]. Hyperlipidemia associated with urolithiasis was significantly reverted back to normal by an aqueous suspension of the aerial parts at a dose of 2 g/kg body weight. This was associated with a decrease in the liver, kidney and serum levels of total lipids, total cholesterol and triglycerides alongwith a reduction in LDL, VLDL, HDL and LDL/HDL ratio [50]. The fruit juice and seed extract showed good inhibition of the mineralization of calcium oxalate, calcium carbonate and calcium phosphate *in vitro* [51]. A dose of 2 g/kg body weight of the aqueous suspension reduced the urinary levels of stone promoters such as oxalate, calcium, uric acid, phosphorus and protein and increased the content of stone inhibitors citrate and magnesium. The oxalate synthesising enzymes that is, lactate dehydrogenase and glycolic acid oxidase also lessened in the liver and kidneys. The histopathological studies showed dissolution of calcium oxalate stones compared to disease control group [52]. The aqueous decoction of leaves at a dose of 3 ml/kg body weight showed significant anti-urolithic activity in ethylene glycol induced male albino rats as supported by the normalisation of urinary markers of stone forming and stone inhibiting constituents. However, the combined regimen of *Aerva lanata* (3 ml/kg body weight) and VEDIUPPU CHUNNAM (3.5 mg/kg body weight) was found to be more effective [53].

### ➤ Nephroprotective activity

The ethanolic extract showed nephroprotective activity against mercuric chloride induced nephrotoxicity in male albino rats. A dose of 200 mg/kg and 400 mg/kg decreased the serum levels of urea, uric acid, creatinine, SGPT, SGOT, alkaline phosphatase and cholesterol whereas, the protein levels increased. There was also an increase in the vitamin C, glutathione content and antioxidant enzymes such as glutathione peroxidase, superoxide dismutase, catalase, glutathione S-transferase in the kidneys and livers of extract treated groups. This was further confirmed by histopathology of the liver and kidneys showing the absence of fatty infiltration, fatty degeneration and necrosis [54]. The ethanolic extract at a dose of 75, 150 and 300 mg/kg decreased the elevated levels of blood urea and serum creatinine in cis-platin and gentamicin induced renal toxicity in male albino

rats in a dose-dependent manner. Histopathological characteristics in the kidneys of intoxicated animals like glomerular congestion, tubular casts, epithelial desquamation, interstitial edema and inflammatory cells were normalized to a considerable extent in animals treated with various doses of extract [55].

### ➤ Antidiabetic activity

A significant antihyperglycemic activity was exhibited at a dose of 200 mg/kg and 400 mg/kg body weight by the methanolic and aqueous extract of the aerial parts which showed a decrease in the levels of fasting blood glucose, serum total cholesterol and triglycerides, SGOT, SGPT, creatinine, alkaline phosphatase, BUN and a reduction in body weight while the total bilirubin was found to increase [56]. The alcoholic extract of the leaves (400 mg/kg) demonstrated a decrease in serum glucose level and a reduction in the body weight of alloxan induced diabetic mice was also avoided. There was an increase in glucose threshold as shown by Oral Glucose Tolerance Test [57]. The ethanolic extract of the aerial parts was studied for its antidiabetic effect in normal and alloxan induced diabetic rats (50, 100 and 200 mg/kg body weight). There was a significant dose-dependent decrease in blood glucose level, body weight and various biochemical parameters such as cholesterol, urea, creatinine, bilirubin and SGPT [58]. The alkaloid basified toluene fraction from the methanolic extract of the roots (10 and 20 mg/kg) showed a lowering of the serum glucose level of streptozotocin-nicotinamide induced type-II diabetic rats along with a raise in glucose threshold, reduction in body weight, total cholesterol, VLDL and LDL [59]. The secondary complications of diabetes induced by streptozotocin in male albino Sprague-Dawley rats was alleviated by the ethanolic extract (250 and 500 mg/kg body weight) as evidenced from boosting of fasting blood glucose and improvement of plasma insulin level, decrease in HbA1c and aldose reductase. An increase in the activity of antioxidant enzymes, that is, superoxide dismutase and glutathione peroxidase was also observed in the liver and kidney alongwith an improvement in the decreased glutathione levels and the glycogen level in liver and muscle. Histopathological studies showed a recovery of the beta cell structure compared to diabetic control which showed a degranulation of beta cells and karyolysis [60]. The ethanolic extract inhibited rat intestinal alpha glucosidase (IC<sub>50</sub>-108.7 µg/ml), increased glucose uptake mediated by insulin (100 µg/ml) and also exhibited antihyperglycemic activity in sucrose loaded streptozotocin normal and diabetic rats (100, 250 and 500 mg/kg body weight) [61]. A decrease in the blood sugar level, body weight, lipid peroxides in alloxan induced diabetic rats was observed with alcoholic extract (250, 375 and 500 mg/kg body weight) [62].

### ➤ Diuretic activity

The methanolic extract of the roots (200 mg/kg) was evaluated for its diuretic activity in male Wistar strain albino rats by Lipschitz method where there was an increase in urine output compared to the control group. However the sodium, potassium and chloride ion excretion were not significantly affected [63]. Alcoholic extract of the powdered shoots showed a diuretic effect in a dose dependent form and also exhibited aquaretic, kaliuretic and chloruretic activity (400 and 800 mg/kg). The sodium and potassium ratio was reduced as half fold [64]. The hydroalcoholic extract of the

flowers (200 mg/kg, 400 mg/kg, 800 mg/kg and 1600 mg/kg) was screened for its diuretic activity for which Lipschitz test was followed. There was increase in urine volume and Na<sup>+</sup>, K<sup>+</sup> and Cl<sup>-</sup> ions in treated group as compared to the vehicle treated group [65]. The ethanolic extract of the mature plants were compared for its diuretic activity (200 and 300 mg/kg) with *Aerva tomentosa* in healthy albino rats by the Lipschitz method. There was an increase in urine output, sodium, potassium and chloride levels in urine with *Aerva lanata*. The alcoholic extract of *Aerva lanata* only gave diuretic activity which was not in *Aerva tomentosa* as compared to standard diuretic drug furosemide [66].

#### ➤ Antimicrobial activity

The ethanolic and ethyl acetate extracts of the stem were tested for their antibacterial activity using agar well diffusion method. A dose dependent antibacterial activity was shown against the microorganisms (500, 750 and 1000 µg/ml). A dose dependent zone of inhibition was observed and the activity was exhibited by the extracts (1000 µg/ml) against gram positive bacteria such as *Staphylococcus aureus*, *Bacillus subtilis*, and gram negative bacteria such as *Escherichia coli*, *Klebsiella pneumonia* strains was more compared to the standard drug, gentamycin [67]. The ethyl acetate and n-butanol fractions derived from the hydroalcoholic extract of the whole plant were evaluated for their antimicrobial activity by preparing serial dilutions using ciprofloxacin as standard (10 µg). Ethyl acetate fraction showed susceptibility against *E.coli* (100 µg/ml), *Bacillus* species (100 µg/ml and 50 µg/ml), *S.aureus* (100, 50 and 25 µg/ml) and *Proteus* species (100 µg/ml) while n-butanol fraction exhibited susceptibility against *Bacillus* species, *S. aureus* and *Proteus* species (100 µg/ml) [68]. The methanolic extract of the plant showed antimicrobial activity (20 µl) against *Mycobacterium phlei* when evaluated by disk diffusion assay [69]. Antifungal activity of the salts from *Aerva lanata* was tested against *Candida albicans*, *Cryptococcus neoformans* and *Aspergillus flavus* through disc diffusion method. The maximum activity was exhibited against *Cryptococcus neoformans*, *Candida albicans* followed by *Aspergillus flavus* (Minimum Inhibitory Concentration of 5 mcg for *Cryptococcus neoformans*, 10 mcg for *Candida albicans* and 20 mcg for *Aspergillus flavus* respectively) [70]. The silver nanoparticles prepared from aqueous extract of the leaves (100 ppm) showed an admirable activity against Methicillin-Resistant *Staphylococcus aureus* [71]. The antimicrobial activity of the aqueous and methanolic extracts of the plant was studied using paper discs method. The aqueous extract showed inhibition against *E.coli* and *Salmonella* species at a concentration of 50 and 100 mg/ml and no inhibition against *Shigella sonnei* whereas, the methanolic extract did not showed any inhibition against any of these Gram negative bacteria [72]. The chloroform extract prepared from the flowers were tested for its antimicrobial activity by agar disc diffusion method against both the clinical and fish-borne microorganisms. Maximum activity was shown against *Aeromonas hydrophila*, *Vibrio alginolyticus* and *E. coli* and minimum antimicrobial activity was observed against *Klebsiella pneumoniae*, *Plesiomonas shigelloides*, *Vibrio cholerae* and *Salmonella paratyphi* when assayed with 100 µl/ml w/v of the extract. Medium activity was observed against *Vibrio mimicus* and *Vibrio harveyi*, the fish-borne pathogens [73]. *Streptococcus mutans* showed susceptibility to the ethanolic extract prepared from the leaves (Minimum

Inhibitory Concentration of 400 mg/ml) [74]. The methanolic extract of the plant exhibited antimicrobial activity against *Xanthomonas campestris* (MIC of 32 µg/ml) and *Aeromonas hydrophila* (MIC of 64 µg/ml) when tested by disc diffusion method [75]. The acetone extract of the leaves showed antifungal activity against *A. niger*, *C. neoformans*, *Fusarium species* and *Nocardia species* when compared to standard, nystatin. It also showed antibacterial activity against *E.coli*, *P. aeruginosa*, *S. typhi*, *S. flexneri*, *S. aureus* and *V. cholerae* when streptomycin was used as standard [76]. The petroleum ether, ethyl acetate and methanolic extracts of the whole plant exhibited significant antibacterial activity against a range of gram negative bacteria (*E.coli*, *Shigella sonnei*, *Shigella dysenteriae*, *Shigella shiga*, *Shigella boydii*), gram positive bacteria (*Bacillus subtilis*, *Bacillus cereus*) while the methanolic and ethyl acetate extracts showed antifungal activity against *Aspergillus niger* and *Candida albicans* compared to standard drug kanamycin [77]. *B. subtilis* and *S. aureus* showed susceptibility to the methanolic and aqueous extracts of the aerial parts when evaluated by broth dilution method using tetracycline as standard [78].

#### ➤ Antioxidant activity

The aqueous, ethanolic and aqueous ethanolic extracts of the plant were tested for antioxidant activity which included DPPH, super oxide anion, hydroxyl radical, nitric oxide radical, hydrogen peroxide radical, total antioxidant capacity assay and anti-lipid peroxidation activity. A concentration of 2.5 mg/ml gave the strong radical scavenging activity. The hydroalcoholic extract gave potent antioxidant activity compared to aqueous and ethanolic extracts. The extracts were found to contain antioxidant compounds like flavonoid, total phenols, tannin, carotenoids and lycopene [79]. *Aerva lanata* showed antioxidant activity when evaluated by DPPH assay which can be attributed to the existence of antioxidants in it [80]. The 50% ethanolic extract was found to possess a reasonable amount of enzymatic antioxidants such as superoxide dismutase, catalase, glutathione peroxidase, glutathione S transferase, peroxidase, ascorbate oxidase, peroxidase, polyphenol oxidase and non-enzymatic antioxidants such as Vitamin C, reduced glutathione [81]. The methanolic extract of the leaves was analysed by DPPH radical scavenging activity, total phenol and flavonoid content determination and reducing capacity assays for testing its antioxidant activity. DPPH assay showed a medium antioxidant capacity of the extract in a dose dependent manner (IC<sub>50</sub> value of 397.24 µg/ml). The phenolic content can be related to its antioxidant activity and a reasonable amount of the flavonoid was also present. A moderately strong reducing power was shown [82]. The methanolic extract of the whole plant was evaluated for its total antioxidant capacity by ABTS, DPPH and FRAP assays and its total phenolic content was also determined and the results were found to be related to each other [83]. A polyherbal formulation of *Aerva lanata* was studied for its antioxidant activity on streptozotocin induced oxidative stress in male Wistar rats. A dose of 500 mg/kg body weight showed enhanced levels of antioxidant enzymes such as superoxide dismutase, catalase, glutathione peroxidase, reduced glutathione and reduced lipid peroxidation [84]. A reasonable *in-vitro* antioxidant activities like superoxide radical-scavenging activity, hydroxyl radical-scavenging activity and DPPH radical-scavenging activity was exhibited by the ethanolic extract of the leaves and the chloroform and hexane fractions derived from it out of which the ethanolic

extract was found to be better. The superoxide radical-scavenging activity gave an IC<sub>50</sub> value of 219.65 µg for the extract, 223.72 µg in case of hydroxyl radical-scavenging activity and 168.13 µg in case of DPPH radical-scavenging activity [85]. The aqueous extract of *Aerva lanata* stem showed high DPPH radical scavenging activity (IC<sub>50</sub>=110.74 µg/ml), metal chelating activity (IC<sub>50</sub>=758.17 µg/ml), reducing power activity in a dose dependent manner and protection against damage to DNA (50 µg) [86]. A powerful DPPH free radical scavenging activity, reducing power capacity and nitric oxide scavenging activities (250 µg/ml) were shown by the methanolic and aqueous extracts in a dose dependent manner compared to standard ascorbic acid [78].

#### Anticancer and antitumor activity

The aqueous extract of *Aerva lanata* was studied for its cytotoxicity by brine shrimp lethality bioassay. The Minimum Lethal Concentration of brine shrimp lethality (LC<sub>50</sub>) of *Aerva lanata* was found to be 77.95 ± 0.62 ppm which was less than the positive control (quinoline), thus proving its higher cytotoxicity [80]. The methanolic extract of the aerial parts were evaluated for its anticancer activity against Ehrlich Ascites Carcinoma (EAC) cells in Swiss albino mice. The various parameters checked were tumor weight measurement, survival time and tumor cell growth inhibition. Brine shrimp lethality bioassay was carried out to test the *in vitro* cytotoxicity and it exhibited moderate cytotoxic activity (LC<sub>50</sub>=23.06 µg/ml). A dose of 40 mg/kg/day (i.p) of the extract decreased the tumor weight, increased the life span and reduced the tumor cell growth rate compared to animals receiving no extract [82]. A polyherbal formulation containing *Aerva lanata* was studied for its antitumor activity in ascites and solid tumors induced by DLA cells in Swiss albino mice. A dose of 2.5 g/kg body weight raised the life span, decreased the solid tumors and the tumour volume was also significantly decreased [87]. The various fractions of the ethanolic extract of the aerial parts were studied for their anticancer activity *in vitro* by sulphorhodamine B (SRB) assay. Five different human cell lines were taken for the study of lung, leukaemia, prostate, colon and cervix cancer. The chloroform fraction demonstrated considerable inhibitory effect for leukaemia, lung and colon cancer (100 µg/ml) against the standard mitomycin while the ethyl acetate fraction exhibited inhibitory effect for lung and cervix cancer (100 µg/ml) when 5-fluorouracil was used as the standard [88]. A pentahydroxy pimarane diterpenoid and twelve other chemical constituents isolated from the methanolic extract of the aerial parts were studied for their cytotoxicity against five cancer cell lines (CHO, HepG2, HeLa, A-431 and MCF-7) using MTT assay employing the standard drug doxorubicin. Amongst the various isolated compounds, canthin-6-one, methylaervine and 3-cinnamoyltribuloside showed favourable activity which can be confirmed from their IC<sub>50</sub> values [89]. Cytotoxicity was observed with partially TLC-purified fraction derived from petroleum ether extract of the whole plant to Dalton's lymphoma ascites (DLA), Ehrlich ascites (EA) and B16F10 cell lines *in vitro* (10-50 µg/ml). The fraction was used to evaluate its ability to decrease the solid tumor induced by DLA cell lines in mice as it proved to be more toxic to DLA cell lines, and the progress of solid tumor in mice was decreased at a dose of 100 mg/kg [90]. Ethanolic extract of the whole plant was tested for its

antitumor activity against Dalton's lymphoma ascites (DLA) and Ehrlich ascites carcinoma (EAC) and was found to be 100% cytotoxic to the cells (500 µg/mL). Cytotoxicity was found towards L929 and HELA cells at higher concentrations. A dose of 10 mg/kg body weight led to decrease in solid tumor development in mice induced by DLA and raised the life span of EAC tumor bearing mice by 53.47% [91]. The ethanolic extract of at a dose of 10 mg/kg body weight prevented formation of tumor nodule in the lungs and enhanced the rate of survival when evaluated for antimetastatic ability by B16F-10 melanoma-induced lung metastasis model [92].

#### ➤ Hepatoprotective activity

The petroleum ether and methanolic extracts of the roots, stem bark and leaves as well as the bioactive compounds isolated from the petroleum ether fraction were evaluated for their hepatoprotective activity using carbon tetrachloride induced hepatotoxicity in albino rats. The extracts and the phytoconstituents at a dose of 200 and 300 mg/kg reduced the raised serum marker enzymes (alanine transaminase, aspartate aminotransferase and alkaline phosphatase) and also decreased the bilirubin level [93]. Hepatoprotective effect of a biherbal ethanolic extract made up of equal quantities of leaves of *Aerva lanata* and *Achyranthes aspera* was studied against hepatotoxicity induced by paracetamol in albino rats. A dose of 200 and 400 mg/kg reduced the increased levels of serum glutamic pyruvic transaminase (SGPT), serum glutamic oxaloacetic transaminase (SGOT) and alkaline phosphatase. A decrease in serum bilirubin and urea with increase in total protein, total cholesterol and triglycerides was also observed. There was also a decrease in liver weight in animals treated with extract [94]. The petroleum ether fraction of the whole plant was tested for hepatoprotective effect against carbon tetrachloride induced liver damage in Sprague Dawley rats. The fraction at a dose of 50 and 100 mg/kg body weight minimised the histopathological changes and corrected the elevated activities of hepatic marker enzymes (glutamate oxaloacetate transaminase, glutamate pyruvate transaminase, alkaline phosphatase) and increased the activities of antioxidant enzymes (catalase, superoxide dismutase, glutathione-S-transferase, glutathione peroxidase, glutathione reductase). There was also a reduction in hepatic lipid peroxidation and an enhancement of the total protein in serum and albumin/globulin (A/G) ratio [95]. The hydroalcoholic extract was evaluated against paracetamol induced hepatotoxicity in rats. A dose of 600 mg/kg protected the liver as seen from the decrease in serum enzymes alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and bilirubin [96].

#### ➤ Immunomodulatory activity

The partially purified fraction derived from the petroleum ether extract of the whole plant was evaluated for its immunomodulatory activity *in vitro* using Daltons lymphoma ascites (DLA) tumor cell lines and on DLA bearing mice *in vivo*. With 50 and 100 mg of the fraction there was a 53% and 73% increase in proliferation in contrast to control (42%) when subjected to lymphocyte proliferation assay *in vitro*. At a dose of 100 mg/kg body weight, the fraction caused a raise in the haemoglobin, WBC count, lymphocytes and eosinophils along with a raise in the lifespan in the treated group in comparison to the disease control [97].

The ethanolic extract of whole plant was evaluated for its immunomodulatory activity and an increase in the total WBC count, bone marrow cellularity, and number of  $\alpha$ -esterase-positive cells was observed at a dose of 10 mg/kg body weight. An increased generation of splenocytes, thymocytes, and bone marrow cells was observed *in vitro* and *in vivo* in the presence and absence of specific mitogens with a raise in the number of plaque-forming cells (PFC) in spleen and circulating antibody titer [91]. A stimulation of cell-mediated immunological responses in normal and tumor-bearing BALB/c mice was observed with ethanolic extract at a dose of 10 mg/kg body weight along with an increase in the natural killer cell activity. An increase in the antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent complement-mediated cytotoxicity (ACC) was also seen. An increased generation of mouse interleukin (IL)-2 and interferon (IFN)-gamma was achieved *in vivo*. An enhancement in cytotoxic T-lymphocyte (CTL) generation was observed in both *in vivo* and *in vitro* when evaluated by Winn's neutralization assay as evidenced by a raise in the life spans of tumor-injected mice [98]. A  $\beta$ -carboline alkaloid, 10-methoxycanthin-6-one, isolated from the ethanolic extract of the whole plant was evaluated for immunomodulatory activity in Balb/c mice. The compound increased the total WBC count, bone marrow cellularity, and number of  $\alpha$ -esterase-positive cells at a dose of 0.5 mg/kg body weight along with an increase in the circulating antibody titer and the number of plaque-forming cells (PFC) in the spleen. A decrease in the mRNA levels of inducible nitric oxide synthase 2, tumor necrosis factor alpha (TNF)- $\alpha$ , and interleukin (IL)-1 $\beta$  and IL-6 in LPS-stimulated macrophages was also observed [99].

#### ➤ Antidiarrhoeal activity

The alcoholic extract of the whole plant was studied for its antidiarrhoeal activity using castor oil induced diarrhoea, charcoal meal test and PGE2 induced diarrhoea. In castor oil induced model, doses of 400 and 800 mg/kg of the extract postponed the defecation time and a decrease in the mean wet defecation was also observed in comparison to the control. There was an obstacle in the onset time and severity of induced diarrhoea. In the charcoal meal study, a reduction in the propulsive motion of charcoal was seen, thus exhibiting a medium antidiarrhoeal effect. In PGE2 induced enteropooling, a reduction in the secretion of intestinal fluid and a protection against PGE2 induced enteropooling was observed [100]. The alcoholic and aqueous extracts were compared for their antidiarrhoeal effect using castor oil induced model. The extracts at 400 and 800 mg/kg exhibited diarrhoeal protection and the aqueous extract showed better activity than the alcoholic extract [101]. A dose of 800 mg/kg of the ethanolic and aqueous extracts of *Aerva lanata* and *Aerva javanica* were studied for their action on intestinal transit which was decreased in charcoal meal test thus showing a considerable antidiarrhoeal activity [102].

#### ➤ Anthelmintic activity

The anthelmintic activity against *Pheretima posthuma* was studied using the methanolic and aqueous extracts of the aerial parts. The activity was seen in a dose dependent manner with both the extracts and a concentration of 100 mg/ml showed the shortest time of paralysis and death of worms and the methanolic extract was found to be more effective [103]. The anthelmintic activity of the aqueous and alcoholic extracts of the stems and leaves was evaluated

against tapeworms and earthworms. The extracts were used in doses of 2.5, 5, 10 and 20 mg/ml and a dose dependent activity was observed. With regard to the time taken for paralysis and death of worms, an improved activity was observed with the ethanolic extract of both the leaves and stems compared to the standard albendazole [104]. The aqueous extracts of *Aerva lanata* and *Rotula aquatica* were compared for their *in vitro* anthelmintic activity on *Pheretima posthuma* where piperazine citrate was used as the standard drug. The parameters considered were the time of paralysis and time taken for death of the worms. The extracts showed activity in a dose dependent way with various concentrations of 25, 50 and 75 mg/ml and the aqueous extract was more active compared to *Rotula aquatica* [105].

#### ➤ Antiinflammatory, analgesic and antinociceptive activity

Carrageenan-induced rat hind paw edema method was used to observe the antiinflammatory activity of the alcoholic extract of the shoots. An inhibition of paw volume was observed at a dose of 800 mg/kg, when ketorolac tromethamine was used as the standard [64]. The hydroalcoholic extract of the flowers were tested for analgesic and antiinflammatory activity using tail immersion method and carrageenan-induced paw edema in albino rats respectively using diclofenac sodium as standard. A significant increase in the reaction time and a decrease in the paw volume was observed at a dose of 400 mg/kg and 800 mg/kg of the extract [65]. The petroleum ether, ethyl acetate and ethanolic extracts of flowers were evaluated for their analgesic activity by tail immersion method and anti-inflammatory activity by carrageenan induced paw edema method with diclofenac sodium and indomethacin as standard drug respectively in wistar rats. The ethanolic extract was found to be more effective compared to other extracts at a dose of 800 mg/kg body weight [106]. The hydroethanolic extract of the aerial parts was evaluated for its antinociceptive effect using acetic acid-induced abdominal writhing and hot plate test on Swiss albino mice. The extract exhibited antinociceptive effect in a dose dependent manner. A noteworthy anti-nociceptive activity was observed at a dose of 100 mg/kg predictable to aspirin. An elongation of the latency period was also observed predictable with morphine. The anti-nociceptive activity of *A. lanata* was not antagonized by naloxone, which was chosen as the opioid receptor antagonist [107]. Stigmasterol-3-glycerol-2'-linoleate, campesterol and daucosterol isolated from the methanolic extract of the aerial parts were observed for their antinociceptive activity at a dose of 100 and 200 mg/kg body weight in mice by acetic acid induced writhing method and tail immersion method. A significant activity was observed with all the compounds in acetic acid-induced writhing method (peripheral analgesic activity) and in tail immersion method (central analgesic activity). The analgesic effect was observed in a significant manner at 180 min and in a moderate manner at 120 min in comparison to control [108].

#### ➤ Antifertility activity

The antifertility activity of the ethanolic extracts prepared from the roots and aerial parts was studied *in-vitro* by anti-implantation, abortifacient, and motility of rat spermatozoa models. At the dose of 200 and 400 mg/kg body weight, a pre-implantation loss of 20% and 30% was exhibited as compared to the control along with a pregnancy failure of

30% and 40% respectively. There was no movement of rat spermatozoa within 60 seconds of administration of 10% concentration of the extract [109].

#### ➤ **Antiulcer activity**

Ethanol, pyloric ligation, indomethacin and cysteamine induced ulcer models were used to study the antiulcer activity of the aqueous extract of the stem in wistar albino rats using omeprazole as the standard drug. A dose dependent activity was exhibited. At 500 mg/kg, a significant reduction in the ulcer index was observed against the control in all the models. There was a reduction in free-acidity and total-acidity alongwith a raise in the pH in pylorus ligated model [110].

#### ➤ **Antiasthmatic activity**

The antiasthmatic activity of the ethanolic extract of the aerial parts was studied *in-vitro* using the isolated goat tracheal chain preparation model at a concentration of 100 µg/ml. The *in-vivo* study was conducted on clonidine-induced catalepsy model and mast cell degranulation in mice at a dose of 30 & 60mg/kg. A dose-dependent effect was observed and the contractions generated by histamine were reduced in the treated group in isolated goat tracheal chain preparation against the control. A prevention of clonidine induced catalepsy was observed. A considerable protection against mast cell degranulation induced by clonidine was also found alongwith mast cell stabilisation (60mg/kg) [111].

#### ➤ **Anti-HIV activity**

The hexane, chloroform, ethyl acetate, acetone and methanol extracts of the roots were observed for HIV-1 reverse transcriptase inhibitory activity by HIV-1 Reverse Transcriptase Inhibition assay. Although, the extracts showed observable activity but maximum inhibition was exhibited by the chloroform and methanolic extracts (2mg/ml) as compared to the control drug, azidothymidine. IC<sub>50</sub> of all extracts was under 40mg/ml [112].

#### **Plant Tissue Culture Studies**

An efficient procedure was set for large scale micropropagation and conservation of *Aerva lanata*. A complete regeneration of the plant was observed after successive subculture in L<sub>2</sub> media. Callusing, shoot multiplication and rhizogenesis occurred when leaf segments and shoot tips were used as explants. The medium which was standardized to be most reasonable for maximum shooting and rooting were L<sub>2</sub> media supplemented with 2,4-dichlorophenoxyacetic acid (2.5 mg/L) and benzylaminopurine (1.5 mg/L) and half strength L<sub>2</sub> media with naphthalene acetic acid (2 mg/L) respectively [113]. An adequate and simple method was developed for using nodal explants for propagation of the plant. Multiple shoot induction through direct organogenesis was perfectly attained with an amalgamation of N<sup>6</sup>-benzyladenine and kinetin (3 mg/L each) in Murashige and Skoog's medium. Maximum shoots were generated through callus mediated organogenesis by supplementing the medium containing the ideal blend of N<sup>6</sup>-benzyladenine and kinetin with α-naphthalene acetic acid (1.0 or 1.5 mg/L). The medium at half the strength containing indole butyric acid was used for rooting the shoots produced. A survival rate of 72±4% was obtained, when the plantlets thus regenerated were implanted in the soil [114]. An effective protocol for micropropagation of

*Aerva lanata* was developed. Murashige and Skoog medium fortified with thidiazuron (0.25–2.0 mg L<sup>-1</sup>), sucrose (3 %) and agar (0.8 %) was employed for deriving *in vitro* plantlets whose leaf segments were used for regeneration. The medium containing thidiazuron (1.0 mg L<sup>-1</sup>) produced the maximum shoot development which generated flowers *in vitro* on a medium consisting of thidiazuron (1.0 mg L<sup>-1</sup>) combined with α-naphthaleneacetic acid (0.25–0.5 mg L<sup>-1</sup>). A high percentage of the regenerated shoots (86%) formed roots and plantlets when shootlets were shifted to half strength MS medium with indole-3-butyric acid (1 mg/L) [115].

**Conclusion:** The present compilation provides sufficient support with regard to the usefulness of this valuable medicinal plant. The various pharmacological activities are attributed to the boundless coverage of various phytochemicals that the plant possesses. Further research is imperative with respect to the biological activities and possible modes of action of the various isolated phytoconstituents. Additionally, toxicological studies in animals need to be carried out so as to proceed to further clinical studies in humans. There is a further scope of development of formulations that can be marketed and employed effectively in combating various disorders.

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