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DISTINCTIVE PHARMACOLOGICAL ACTIVITIES OF *Eclipta alba* AND IT'S COUMESTAN WEDELOLACTONE

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Abstract:

Eclipta alba Linn. (Eclipta prostrata) is a perennial herb belongs to the family Asteraceae which is widespread all over the world especially in south Asian countries like India, Nepal, China and Thailand. Because of its numerous pharmacological activities, it is used in Siddha, Unani and Ayurveda to treat skin infections, headache, toothache and other such ailments. It possess anti-inflammatory, anti-fibrotic, anti-osteoporotic, anti-cancer and hepatoprotective activities due to the phytochemicals like dimethyl wedelolactone and wedelolactone present in it. The coumestan wedelolactone has potent activity against human pathogens like

Bacillus subtilis, Pseudomonas aeruginosa, E.coli and Salmonella typhi. We pen down this reviewto investigate the predominant pharmacological activities of coumestan wedelolactone.

Key words: *Eclipta alba , Coumestan, Wedelolactone, Hepatoprotective, anticancer, anti-fibrotic.*

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INTRODUCTION:

Eclipta alba L. is an annual herb in china and many other countries in the world. It is a famous traditional medicine and is also edible natural product. It is used in treatment of hemorrhages, hepative disease renal injuries, hair loss, tooth mobility and viper bites in traditional Chinese medication [1]. (National Commision of Chinese Pharmacopoeia). Modern pharmacological research showed that it exhibits various bioactivities including anti-tumor, anti-snake venom, anti-inflammatory, anti-oxidation, anti-HIV-1 integrase, reduction of blood lipids, and prevention of CCl_4-induced liver damage [2]. Stigmasterol, caffeic acid and wedelolactone have been determined as markers of *E.prostrata L*. Methanol extract of E.prostrata L. have been used to treat jaundice, leishmaniosis mouse osteoblast differentiation and hepatic stellate cell proliferation. In china, 'Kidney-nourishing' herbal drugs including *Eclipta herba* are commonly believed to have the ability of nourishing bones and therefore are used to treat bone diseases such as osteoporosis.

A-terthienyl-methanol, a naturally occurring terthiophene isolated from E.prostrata, induces apoptosis in human endometrial cancer cells by ROS production, partially via NADPH oxidase.

An annual herbaceous plant called *Eclipta Alba (Eclipta prostrata L.)* belongs to the family Asteraceae or compositae [3] found all over the world, especially in the tropical and subtropical areas China, India, Southwestern US, [4] Thailand, Brazil and an auspicious herb in the group of dasapuspam

It has a small branches with white flower heads found in Indian hills about 600 feet ascending and medicinally important herb in the region like Asia, Africa and South America. It grows in moist places via seeds but it is endangered by the pests and diseases in their habitat. Because of its bivariate pharmacological activities, we pen down this review to investigate coumestan Wedelolactone of *Eclipta alba* (EB).

Table 1: Different names of *E.alba*

Terms & names	Known for EB's	Reference
Eclipta prostrate	Synonym	[5]
Ecliptaeherba	Synonym	[6]
Ecliptaerecta, Eclipta alba	Botanical name	[5]

Traditional medicine in various region:

It is an edible natural product and used as a traditional medicine, vegetable dye. As a traditional medicine in china, it acts as a blood enriching tonic, and act against hemorrhages, hepative disease, renal injuries, hair loss, tooth mobility and viper bites. In Asia it acts against hyperlipidemia, atherosclerosis, hepatic disorders, spleen enlargement, and skin diseases. Generally, it is used in the treatment of skin disorders, liver diseases, premature graying of hair, and to enhance the memory. In Ayurveda, it is consider as a reputed herbal medicine and act as a hepato-protective agent & used in the treatment of many liver ailments, hepatitis [7] kapha and vata imbalances jaundice in children. For rejuvenation and longevity it is used as a tonic [8]. In ancient days, it is considered as nervine tonic. In Unani medicine, it is consider as a reputed herbal medicine. In India, it is a pioneer ingredient in anti-hepatotoxic phyto pharmaceutical formulation.

E. alba as dietary food:

As a dietary food, E.alba act against *Aeromanas hydrophila* by improving immune response and disease resistance of *Oreochromis mossambicus* (*Mozambique tilapia*) in fish [9] and also it reduced serum triacylglycerol level in albino rats [10].

E. alba in modern pharmacological activities:

It contains various bioactivities according to modern pharmacological research such as anti-tumor, anti-HIV-1 protease & integrase, blood lipids reduction, and prevent liver damage induced by CCl_4 [11, 2] anti-inflammatory [13], anti-snake venom, [14]. anti-oxidation,[15] anti-nociceptive, bronchodilator activities anti-HCV. Hepato-protective [16] anti-hyperglycemic agent. and used in the treatment of enteritis, hepatitis hyperlipidemia, atherosclerosis, skin diseases, spleen enlargement, gall bladder [17,3] viral hepatitis [18] jaundice, peptic ulcers [19]. guina pigs liver damage induced by CCl_4 [8] hepatic cirrhosis and infective hepatitis. In addition to that, E.alba is widely used in India as a cholagouge and deobstruent in hepatic enlargement, for jaundice and other ailments of the liver and gall bladder. The potential neuro pharmacological activity of the plant E.alba as a nootropic and also having the property of

attenuating stress induced alterations [20]. It also possesses hepatoprotective, hair growth promoting and anti-aging properties.REF. The methanol extract was found to be the most effective for ovicidal activity against Aedesaegypti. The methanol extracts exerted 100% mortality (Zero hatchability) at 300 ppm [9]. The methanol extracts of the whole plant of E.alba significantly increased the phagocytic index, antibody titer and WBC count in mice [6]. *Ecliptaalba* extract (EAE) inhibits the cell proliferation in dose dependent manner in HepG2, A498 and C6 glioma cell lines with an IC50 of 22±2.9, 25±3.6 and 50±8.7 µg/ml respectively. The treatment of milidly hypertensive male with capsulated E.alba powder sowed diuretic, hypotensive, and hypocholesterolemic effects and alleviated complications due to oxidative stress [21].

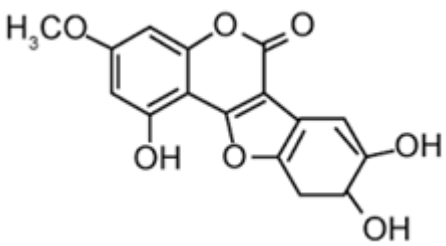
Phytochemicals:

The plant is reported to contain the phyto constituent seclalbatin, alpha-amyrin, ursolic acid and Oleanolic acid *Ecliptasaponin*, daucosterol, stigmasterol-3-o-glucoside and coumestans as main active principles [22]. The herb is rich in ascorbic acid. It is a good source of thiopene derivatives which are effective against nematodes. From this herb, ecliptal. Wedelolactone, dimethyl wedelolactone and its 7-O-glucoside, β-amyrin were isolated [23]. Due to increased pharmaceutical demand, the status of E.alba in the wild has been significantly affected.

Coumestan- Wedelolactone:

The herb *Eclipta alba* contains mainly coumestans [24]. The coumestan Wedelolactone and dimethyl wedelolactone possess potent anti-hepatotoxic activity and is recommended for the treatment of hepatitis and cirrhosis. Comparatively Wedelolactone has more potent activity among the other coumestans.

Wedelolactone Structure:



Wedelolactone as an anti-inflammatory agent:

[10] shows that wedelolactone suppress GPR-35 (the gene responsible for allergic reaction and which is expressed by gallic and caffecic acids) & act as a drug for asthma, this is proved by comparing it with cromolyn disodium in DMR assay. It also detects β – arrestin translocation signals and acts as an agonist [25]. It inhibit lipoxygenase [12] and this is also revealed by [13] but they told that inhibition occur especially in 5' (5'- lipoxygenase) and act as a liver peroxidase inhibitor [26]. IC_{50} values obtained from WE and DMW inhibits trypsin, which causes inflammation.

Wedelolactone as an anti-fibrotic agent:

Earlier studies demonstrate the anti-fibrotic effects of wedelolactone on activated human hepatic stellate cell (HSC) due to the cellular viability of Lx-2 [27]. Wedelolactone might present as a useful tool for the prevention and treatment of hepatic fibrosis. It elucidates the mechanism of the anti-fibrotic effects by wedelolactone on LX-2 cell lines, and is expected to reveal new opportunities for the development of novel therapeutic strategies against liver fibrosis [28].

Wedelolactone as an anti-osteoporotic drug:

Accumulating evidence indicates that extracts of *Eclipta herba* have anti-osteoporotic effect [29]. The effective compounds and cellular mode of action are still unclear. The effect of ethyl acetate extract of *ecliptaherba* [EAE] and its component wedelolactone involves in the proliferation and differentiation of preosteoclastic RAW 264.7 cells as well as proliferation of bone marrow stromal cells [BMSC]. The formation of multinucleated TRAP positive RAW 264.7 cells was observed by using a TRAP – staining kit. Treatment of RAW264.7 cells with EAE at high doses (20 µg/ml and 40 µg/ml) or wedelolactone at 10 µg/ml resulted in decrease in proliferation of RAW 264.7 cells. The inhibitory effect of wedelolactone is more potent than that of alendronate, which is an anti-resorptive drug. Morphological changes revealed that 5 µg/ml EAE and 2.5 µg/ml wedelolactone reduced the number of multinucleated osteoclast-like cells. At the high doses. EAE (20µg/ml) and wedelolactone (10 µg/ml) inhibited the growth of BMSC. EAE and its component wedelolactone inhibited osteoclast RAW 264.7 proliferation and differentiation at the low doses, but at the high doses, showed cytotoxic effect of BMSC. There results indicated that EAE and wedelolatone might be potential alternative therapy for osteoporosis. Data suggest that EAE as well as its component wedelolactone have the potential to serve as therapeutic intervention for skeletal diseases associated with bone loss [24].

Wedelolactone as an anti-cancer agent:

As a result of pathological stimulation there involves IL-1β maturation and apoptosis (pathological) in the presence of LPS [30]. It is inhibited by wedelolactone by suppression of IKK that further inhibits NF-κB mediated transcription. Inhibition of NFκB and

androgen receptors by wedelolactone at different phases of cell cycle such as S/G2/M does not tend to inhibit negative breast cancer cells. It also induces DNA damage signaling and on interaction with dsDNA it inhibits the activity of DNA topoisomerase Iiα [31]. The new derivative from wedelolactone namely BTB which selectively inhibits ER activity and have the potential to treat breast, endometrial and ovarian cancers due to its 17-estradiol (E2) induced ER transactivation, in ER positive cells at the concentration of 2.5μM. i.e., suppression of E2 mediated ER target genes (cyclin D1, E2F1, and TERT), & in case of ER +ve cells (MCF-7, SKOV-3) [13]. Wedelolactone is tend to have anti-cancer activity. The main targets involved are multiple cellular proteins such as androgen receptors, 5-lipoxygenase and topoisomerase IIα iv-vivo. In the case of breast cancer, as a phytoestrogen it stimulates the expression of genomic and non-genomic ER positive cell-signaling, thus acting as an agonist to breast cancer, except in ER negative cancer cells. The polyphenolic compound wedelolactone is involved in inhibition of topoisomerase II-α i.e., it does not allow the plasmid DNA to bind with topoisomerase II-α which is a redox dependent reaction. In some occasions when the enzyme level is high it might not happen. MDA-MB 231 AND 468 both partially inhibited wedelolactone, as the former inhibits the catalase also, even though wedelolactone is involved in DNA damage in breast cancer cells. All these events are found to happen at the redox state. The hydro alcoholic extract of extract of *Eclipta alba* inhibits the cell proliferation in HepG2 (IC5022±2.9), A498 (IC50 25±3.6), C6 glioma cell lines(IC50 50±8.7) and proves as anti-proliferative anti-invasive and apoptic nature of HAE of E.alba also the expression of Matrix metalloproteinases were down regulated (MMP 2&9). In human ovarian cancer cells (SKOV3 and A2780), *Eclipta alba* saponin II induces autophagy by suppressing mTOR and activates MAP kinase JNK and p38 signaling pathways [14]. Wedelolactone and Dimethyl wedelolactone shows anti-invasive effect in human breast cancer cells (MDA-MB-231) by suppressing the expression of matrix metalloproteinases (MMPs) that helps in blocking IkB-a/NFkB and MEK/ERK signaling pathways [16]. The proliferation of hepatoma cell smmc-7721 is inhibited by 30% ethanol fraction and E. alba saponin I obtained from *Eclipta prostrate* (IC50 values 74.2399 and 111.1703 mg/ml), tend to possess anti-tumor activity.

As a hepato-protective agent:

Theethanolic extract of *Eclipta alba* has a well anti-HCV activity [32]. By examine, the extract it consists of a major compounds like Wedelolactone and it is isolated. The activity has well executed in in vitro and in cell culture system. So the result shows a clear report, that *Eclipta alba* has a well complementary treatment against Hepatitis C virus [33].

Anti-microbial agent:

The methanolic extracts of *Eclipta alba* were tested against nine microbial species to show the antimicrobial activity by well diffusion method [34]. By the analysis, the N-butanol extracted sample showed high inhibitory activity against all the nine microbial species. But also different extracted samples show varying inhibitory activity against microbial species [35, 36]. Here, the most resistant microbial strain was *Salmonella typhi.* The most resistant Gram-positive bacteria was *Bacillus cereus* and the most resistant Gram-negative bacteria was *E.coli* and *Salmonella typhi.* And also the crude methanol extract showed effective against Antifungal activity. Ray. A *et al.*, says that the extracted Eclalba saponin from *Eclipta alba* shows a great Antibacterial activity against both *Bacillus subtilis* and *Pseudomonas aeruginosa* with an inhibition pH range of 5.5-9.0. Also, the antibacterial activity was performed by using gel diffusion technique and Crystal violet assay. And the result showed a great effectiveness against Gram-positive and Gram-negative bacteria. And also, the extracted saponin was found to have a high bactericidal activity. [37] Says that the extract of *Eclipta alba* shows a great Antibacterial activity against the different six bacterial strains. And also, the phytochemical screening is done to exhibit the different compounds such as tannins, flavonoids, coumestans, saponins and alkaloids. Among these, Wedelolactone acts a great promising antimicrobial agent. As, the result shows the *Staphylococcus epidermidis, Staphylococcus aureus* and *Salmonella typhimurium* were more susceptible and *Shigella flexneri*is the resistant bacterial strain. It also responds to actionomycetes [38]

CONCLUSION:

This review contains all the major pharmacological activities of the compounds present in the *Eclipta alba* which leads to the sustainable development of medical and agricultural fields. So it will make the future researcher to work in a different angle in this plant to make new data. Here we imaged the rough & trough of E. alba, so it will be the supportive document for the future researcher to make products out of it. Previously we worked on some Indian traditional medicinal plants like *Solanum trilobactum* [39], Nigella sativa [40], *Ficus recemosa* [41] *Leucas Aspera* [42], *Adhathoda vasica* [43] and *Allium sativum* [44] to give proper scientific evidence.

Moreover this review resembles that wedelolactone of E.alba could be a strong hepato-protective & potent anticancer agent and may be consume as a drug in future.

REFERENCES:

1. Rajakumar G, Abdul Rahman A, Priamvada B, Gopiesh Khanna V, Kishore Kumar D, Sujin PJ. Eclipta prostrate leaf aqueous extract mediated synthesis of titianium dioxide nanoparticles. Materials Letters, 2011; 68:115-117.
2. Santhosh Kumari C, Govindasamy S, Sukumar E. Lipid lowering activity of Eclip*taprostrat*a in experimental hyperlipidemia. Journal of Ethnopharmacology, 2006; 105:332-335.
3. Mansoorali KP, Prakash T, Kotresha D, Prabhu K, Rama Rao N. Cerebroprotective effect of *Eclipta alba* against global model of cerebral ischemia induced oxidative stress in rats. Phytomedicine, 2012; 19: 1108-1116.
4. XinshengFang,JianhuaWang,JifuHao,XuekeLi,NingGuo. Simultaneous extraction,identification and quantification of phenolic compounds in *Eclipta prostrata* using microwave-assisted extraction combined with HPLC-DAD-ESI-MS/MS. Food chemistry,2015;188:527-536.
5. Saxena AK, Singh B, Anand KK. Hepatoprotective effect of *Eclipta alba* on subcellular level in rats. Journal of Ethnopharmacology, 1993; 40: 155-161.
6. Lakshmi Reddy S, Fayazuddin MD, Reddy NCG, Adeel Ahamad, Siva Reddy G, Sambasiva Rao P, Jagannatha Reddy B, Frost RL. Characterisation of bhringaraj and guduchi herb by ICP-MS analysis, optical absorption, infrared and EPR spectroscopic methods. Spectrochimic aActa Part A, 2008; 71:31-38.
7. Christybapita D, Diyagnaneswari M, Dinakaran Michael R. Oral administration of *Eclipta alba* leaf aqueous extract enhances the non-specific immune responses and disease resistance of Oreochromis mossambicus. Fish & Shellfish immunology, 2007; 23: 840-852.
8. Dae-IkKim,Sung-HyenLee,Jin-Ho Choi,Hyun Soon Lillehoj,Mi-HeeYu,Gun-Soon Lee.The butanol fraction of *Eclipta prostrata*(Linn) effectively reduces serum lipid levels and improves antioxidant activities in CD rats. Nutrition Research, 2008; 28:550-554.
9. Jayathirtha MG, Mishra SH. Preliminary Immunomodulatory activities of methanol extract of *Eclipta alba*, and Centella asiatica. Phytomedicine, 2004; 11:361-365.
10. Khin Ma-Ma, Nyunt Nyunt, KhinMaung Tin. The protective effect of *Ecliptaalba*on Carbon tetrachloride-induced acute liver damage. Toxicology and Applied Pharmacology, 1977; 45:723-728.
11. Thakur VD, Mengi SA. Neuropharmacological profile of *Eclipta alba* (Linn.)Hassk. Journal of Ethnopharmacology, 2005; 102:23-31.
12. Govindarajan M, Karuppannan P. Mosquito larvicidal and ovicidal properties of *Eclipta alba* (L.) Hassk (Asteraceae) against Chickungunya vector, Aedesaegypti (Linn.) (Diptera: culicidae). Asian Pacific Journal of Tropical Medicine, 2011; 24-28.
13. Huayn Deng, Ye Fang. Anti-Inflammatory gallic acid and wedelolactone are G protein-coupled receptor-35 agonists. Pharmacology, 2012; 89:211-219.
14. Walter Mors B, Maria Celia Do Nascimento, Jose Paz Parenter, Maria Helena Da Silva, Paulo Melo A, Suarez-Kurtz G. Neutralization of lethal and myotoxic activities of south American rattlesnake venom by extracts and constituents of the plant *Ecliptaprostrata* (Asteraceae). Toxicon, 1989; 27(9):1003-1009, 1989.
15. Archana Gawde J, Paratkar GT. Production and Enhancement of Wedelolactone in shoot cultures of *Eclipta alba*. Journal of Herbs,Spices and Medicinal Plants, 2012; 18:203-209.
16. Defeng Xu, Tzu-Hua Lin, Chiuan-Ren Yeh, Max A, Cheng, Lu-Min Chen, Chawnshang Chang, ShuyuanYeh. The wedelolactone derivative inhibits estrogen receptor-mediated breast, endometrial, and ovarian cancer cells growth. Bio Med Research International, 2014.
17. Jae-SeungLee,Ji-HyeAhn,Yoon-JinCho,Ha-YeongKim,Yeong-In Yang, Kyung-Tae Lee, Dae-SikJang, Jung-Hye Choi.α-Terthienylmethanol,isolated from *Ecliptaprostrata*, induces apoptosis by generating reactive oxygen species via NADPH oxidase in human endometrial cancer cells. Journal of Ethnopharmacology, 2015; 169: 426-434.
18. Chia-Fu Chang. Ling-Yi Yang, Shiao-Wei Chang, Yu-Ting Fang, Yean-Jang Lee. Total synthesis of dimethyl wedelolactone and wedelolactone by Cu-mediated/Pd (0)-catalysis and oxidative-cyclization. Tetrahedron, 2008; 64: 3661-3666.
19. Seyoung Lim, Hyun-Jun Jang, EunHee Park, Jung Kuk Kim, Jung-Min Kim, Eung-Kyum Kim, Kyungmoo Yea, Yun-Hee Kim, Whaseon Lee-Kwon, Sung Ho Ryu, Pann-Ghillsuh. Wedelolactone inhibits Adipogenesis through the ERK pathway in human adipose tissue-derived Mesenchymal stem cells. Journal of cellular biochemistry, 2012; 1113, 3436-3445.

20. Elisa Pocas SC, Daniele Lopes VS, Alcides da silva JM, Paulo Pimenta HC, Fernanda Leitao B, ChaquipNetto D, Camilla Buarque D, Flavia Brito V, Paulo Costa RR, Francosis Noel. Structure activity relationship of wedelolactone analogues. Structural requirements for inhibition of Na+, K+-ATPAase and binding to central benzodiazepine receptor. Biochemistry & Medicinal chemistry, 2006; 14: 7962-7966.
21. wedelolactone, heparin, and para-bromophenacyl bromide to antagonize the myotoxic effects of two crotaline venoms and their PLA_2myotoxins. Toxicon, 1997; 37: 199-215.
22. Shashi Kant Singh, Manoj Rai, LingarajSahoo K. An improved and efficient micropropagation of *Ecliptaalba* through transverse thin cell layer culture and assessment of clonal fidelity using RAPD analysis. Industrial Crops and Products, 2012; 37:328-333.
23. Shoji Yahara, Ning, Ding Toshihiro, Nohara Kazuo, Masuda,Hiroyuki. AgetaTaraxastane glycosides from *Ecliptaalba*. Phytochemistry , 1997;44(1):131-135.
24. Lifeng Han, Erwei Liu, AgyemangKojo, Jing Zhao,WeiLi,YiZhang,TaoWang,Xiumei Gao Qualitative and Quantitative Analysis of *Ecliptaprostrata L*.by LC/MS.The Scientific World Journal Volume ,2015.
25. Sun Zhi-Hua, Zhang Chao-Feng,ZhangMian. A new benzoic acid derivative from *Ecliptaprostrata*. Chinese journal of Natural Medicine, 2010; 8(4):0244-0246.
26. XinshengFang,JianhuaWang,YingziWang,Xueke Li,HongyingZhou,LixiangZhu.Optimization of ultrasonic-assisted extraction of wedelolactone and antioxidant polyphenols from *Ecliptaprostrata L* using response surface methodology. Separation and Purification Technology, 2014; 138: 55-64.
27. AkinoriTabata,MasahikoTaniguchi,MakioShiban o. Ecliptamines A-D, four new guanidine alkaloids from *Eclipta prostrata L*. Phytochemistry Letters, 2015; 11:224-228.
28. Qj-Mei Liu,Hai-Yan Zhao,Xian-KeZhong,Jian-Guo Jiang. *Eclipta prostrata L*. phytochemicals:Isolation,Structure elucidation and their antitumor activity. Food and Chemical Toxicology, 2012; 50:4016-4022.
29. YunZhao,LuPeng,WeiLu,YiqingWang,Xuefeng Huang,ChenGong,LinHe,JunhaoHong,Songsong Wu,XinJin.Effect of *Eclipta prostrata* on lipid metabolism in hyperlipidemic animals. Experimental Gerontology, 2014; 62: 37-44.
30. Padma Vankar S, RakhiShanker, Jyoti Srivastava. Ultrasonic dyeing of cotton fabric with aqueous extract of *Eclipt aalba*. Dyes and Pigments, 2005; 72:33-37.
31. Petr Benes, Petra Alexova, Lucia Knopfova, Alena Spanova, Jan Smarda. Redox state alters Anti-cancer effects of wedelolactone. Enivironmental and Molecular mutagenesis, 2012.
32. Saranya, Kalimuthu J, Balakrishnan P, Ramalingam PS, Parthasarathi S, Ganesan B, Kaliyaperumal R, Ranganathan B, Shanmugam K.Isolation and Characterisation of Cellulolytic Activity Of Bacteria And Fungi From The Soil Of Paper Recycling Unit At PeriyarManiammai University**.** Indo American Journal of Pharmaceutical Research, 2017; 7(5):1-12.
33. Aruna AP, Pursothaman B, Shanmugam K, Rajendran K. Biological Finger Printing Of Microbial Diversity In VermicompostOg Different Raw Materials. Indo American Journal of Pharmaceutical Research, 2017; 7(04).
34. Yan-QiuLiu,Li-Bin Zhan,TiegangLiu,Meng-Chum Cheng,Xiao-Yan Liu,Hong-Bin Xiao.Inhibitory effect of Ecliptaherba extract and its component wedelolactone on pre-osteoclastic proliferation and differentiation. Journal of Ethnopharmacology, 2014.
35. HanLifeng,ZhaoJing,ZhangYi,KojoAgyemang,L iuEr-wei,WangTao.Chemical constituents from dried aerial parts of *Eclipta prostrata*. Chinese Herbal Medicines, 2013; 5(4):313-316.
36. Sundaramoorthi M, Prabaharan C, Purushothaman B, Saravanan TS. Antibacterial And Wound Healing Effects Of Semi Purified Proteins From Certain Selective Slaughter House Animals. Indo American Journal Of Pharmaceutical Research, 2014; 4(01): 1021-1028.
37. Sagar BPS, Rajiv panwar, Ashwini Goswami, KuldeepKadian, Kanchan Tyagi, Manoj Chugh, Sunita Dalal, Zafar R. Pharmacokinetic interactions of antihepatotoxic wedelolactone with paracetamol in wistar Albino rats. Pharmaceutical Biology, 2006; 44:554-561.
38. Padma Singh and Pallavi., Screening of Potential Antibiotic Producing Actinomycetes from the Soil of Ganga River Bed of Haridwar, Indo Am. J. P. Sci, 2018; 05(04).
39. Balakrishnan P, Musafargani TA, Subhramanyam S, Shanmugam K. A prespective on bioactive compounds from *Solanum trilobactum*. J. Chem. & Pharma. Res, 2015; l 7(8):507-512.
40. Ramalingam PS, Monisha AS, Ravichandiran P, Shanmugam K, Nagarasan S, Balakrishnanan P. Lipid peroxidation and anti-obesity activity of

Nigella sativa seeds. World journal of pharmaceutical research, 2017; 6(10):882- 892.
41. Sethuraman J, Nehru H, Shanmugam K, Balakrishnan p. Evaluation of potent phytochemicals and antidiabetic activity of *ficus racemosa linn*. 2017; 6(15):909-920.
42. Nagarasan S, Boominathan M.*Invitro*studies on the primitive pharmacological activities of *Adhatoda vasica.* Int. J. of Life Sciences, 2016; 4 (3):379-385.
43. Nagarasan S, Boominathan M. Perspective Pharmacological Activities of *Leucas Aspera: An Indigenous Plant Species.* Indo American Journal of Pharmaceutical Research, 2016; 6(9):6567-6572.
44. Rathnasamy S, Auxilia LR, Pursothaman B. Comparative studies on Isolation and characterization of Allinase from Garlic and onion using PEGylation-A novel method. Asian J. Chem, 2014; 26(12): 3733-3735.