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An overview on pharmacological actions of *Kalmegh* (*Andrographis paniculata* Nees.)

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ABSTRACT –

As indigenous sources of medications, medicinal plants are used from the most primitive times. Out of these vastly used potential medicinal plants, *Kalmegh* having botanical name *Andrographis paniculata* (Nees), is an annual herbaceous plant of the family Acanthaceae, commonly known as "king of bitters". All parts of this plant are used as medicine but the compositions of phytoconstituents widely differ from one part to another and with place, season, and time of harvest. According to Ayurved *Granthas* kalmegh has *Tikta rasa* with *Katu Vipaka* and *Ushna Veerya*. It is described in *Priyanighantu* in the '*Shatpushpadi Varga'*. It has *kapha-pitta doshahara* properties so it is used in *Yakrutroga, Krimiroga, Kushtha, and Jwara*. .This plant is by tradition used for the treatment of common cold, diarrhoea, fever, jaundice, as a health tonic for the liver and cardiovascular health by tradition and as an antioxidant. It is also used to improve sexual dysfunctions and function as a contraceptive. In this review we will describe the botanical distribution, phytochemical constitution, microscopy and various pharmacological actions.

KEYWORDS – *Kalmegh*, pharmacological actions

INTRODUCTION-

Medicinal plants are the major sources for the therapeutic remedies of various ailments from the ancient era. Their *rasa*, *guna*, *veerya*, *vipaka* and *prabhava* i.e. *pancha padartha* are responsible for these potential medicinal effects. One of such plant called as *Kalmegh* used in ancient oriental and ayurvedic medicine. The genus Andrographis consists of 28 species of small annual shrubs essentially distributed in tropical Asia. [1] Only a few species are medicinal, of which Andrographis paniculata is the most popular. *Kalmegh* is the herbaceous plant, native of all over India. It is

widely cultivated in Southern and Southeastern Asia. It is used to treat infections and some diseases, often being used before antibiotics were created. All parts of this plant are useful for medicinal activities. Andrographis paniculata is well known plant in Bengal by the name *'kalmegh' Kalamegha*, meaning "dark cloud". It is also known as *Bhui-neem*, meaning "neem of the ground", Andrographis and *Kirayat*. [2] The plant is known in north-eastern India as *Maha-tita*, literally "king of bitters" [3] because of its bioactive component Andrographolid which is of *Tikta rasa.*

CLASSIFICATION OF ANDROGRAPHIS PANICULATA

Domain: Eukaryota

Kingdom: Plantae

Subkingdom: Tracheobionta

Superdivision: Spermatophyta

Division: Angiosperma

Class: Dicotyledonae

Subclass: Gamopetalae

Series: Bicarpellatae

Order: Personales

Family: Acanthaceae

Subfamily: Acanthoideae

Tribe: Justiciae

Subtribe: Andrographideae

Genus: Andrographis

Species: A. paniculata (Burm.f.)Nees [4, 5, 6]

VERNACULAR NAMES -

Sanskrit- *Bhunimb, Kalmegh*

Hindi- *Kalmegh, Kalpnath*

Bangali- *Kalmegh, Oli kiriyat*

Gujrathi- *Kiriyatu*

Tamil- *Nelvemu*

Kannad- *Nelveru*

Mallyalam- *Nelvepu*

Farasi- *Naine-havandi*

Urdu- *Bhuinimo*

English- *The Creat, King of Bitters, Kalmegh* [7]

Ayurvedic aspect-

Acharya Priyavrat Sharma mentioned it in the '*Shatpushpadi Varga'*. It is of *Tikta rasa* with *Katu Vipaka* and *Ushna Veerya* and *kapha-pitta doshahara* properties so it is used in *kapha-paittik vikara*. It is prominently used in the diseases of *paachana samsthana, raktavaha samsthana* and *twakroga*. In Priyanighantu, it has been discussed that *Kalmegh* has activities like *Paachana, Swedana, Krimighna* and *Pittasaraka*. So it has been spacious in *Yakrutroga, Krimiroga, Kushtha, and Jwara.* [7]

कालमेघस्तु भूनिम्बो यवाकारफलस्तथा|

सुतिक्तः लघुरुक्षोष्ण कफपित्तविनाशनः||

दीपनः स्वेदनो ज्ञेयः कृमिघ्नः पित्तसारकः|

यकृतरोगे क्रिमी कुष्ठे ज्वरे चासौ प्रशस्यते||

प्रिय निघण्टुः,शतपुष्पादि वर्ग,श्लोक नं.१३५-१३६,पान नं.१००

Morphology of plant-

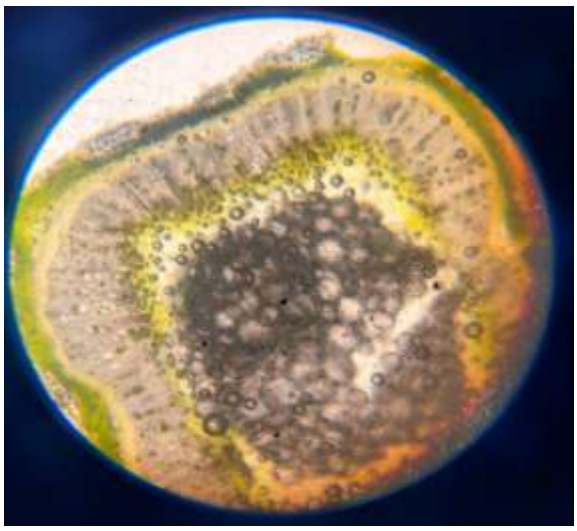
Kalmegh is an annual abundantly branched, erect herb extremely bitter in taste. It grows to a height of 1 to 3 feet in moist shady places with glabrous leaves and white flowers with rose purple spots on the petal. The stem dark green, 0.4-1.0 m in height, 2-6 mm in diameter, quadrangular with longitudinal furrows and wings on the angles of the younger parts, slightly enlarged at the nodes; leaves glabrous, up to 1.5 to 2.5inch long and 0.5 to 0.75 inch broad, lanceolated, pinnate; flowers small and solitary, corolla whitish or light pink in colour with hairs, in lax spreading axillary and terminal racemes; capsules linear-oblong, acute at both ends, 0.75 inch; seeds numerous, sub quadrate, yellowish brown. Flowering and fruiting season appears in September to May.

Distribution -

It is found in Sri Lanka, Pakistan, Java, Malaysia, Indonesia and throughout India, specifically in Maharashtra, Karnataka, Uttar Pradesh, Tamilnadu, Andhra Pradesh and Madhya Pradesh. It is cultivated to some extent in Assam and West Bengal. [8]

Microscopic Examination-

Stem-



In T.S. of stem, quadrangular outline was found with dense collenchyma strands at the four angles of the stem. Epidermis is single layered of rectangular cells. Collenchymas cell zone is a group of 2–3 layered with secretary cavities having white coloured deposition. Cortex forms a narrow zone, composed of 5–6 layers of parenchymatous cells with chloroplast. Solitary sclereids and a group of sclereids of 4–6 are present in the cortex followed by a layer of thick-walled endodermis and parenchyma contains chloroplastid. Solitary sclereids are present in secondary phloem tissues. Xylem occupies the major portion of the stem. Vessels are small sized, mostly solitary and majority of them are arranged in radial rows. Vessels are circular or polygonal shaped. The Diameter of vessel lumen ranges from 18.3 µm to 35.8 µm. Mean number of vessels per square millimetre of the xylem was found to be 393.8 (ranges 419.8 to 345.4). Wood with spiral,

reticulate and pitted xylem vessels were revealed. The vessels with bordered pits and inter vessel pitting were of alternate position were observed. The bulk of the xylem is constituted by fibres. Medullary rays are very exposed and many in number. Rays are mostly uniseriate but occasionally biseriate rays are also found. Polygonal shaped parenchymatous cells are placed with central pith, which contain prismatic crystals of calcium oxalate. [9]

TRADITIONAL USES-

Andrographis paniculata has been reported as having antibacterial, antifungal, antiviral, choleretic, hypoglycemic, hypocholesterolemic, adaptogenic, anti-inflammatory, emollient, astringent, diuretic, carminative, anthelmintic, antipyretic, gastric and liver tonic. It has extremely beneficial activities antioxidant, anti-helminthic, antipyretic, anticancer and antidiarrhoeal effects.[10] .Because of its "blood purifying" activity, it is suggested in cases of *raktapradoshaj vikara* like leprosy, gonorrhoea, scabies, boils and skin eruptions, chronic and seasonal fevers. *Swaras* of leaves is given to infants for the relief in griping, irregular bowel habits, and loss of appetite. Its leaves and roots are also used in general weakness, febrile convalescence, gaseous distension related dyspepsia and in advanced stages of dysentery. Ayurvedic formulations used to treat liver disorders and can be widely used to treat neoplasm as mentioned in ancient Ayurvedic literature. [11, 12] Andrographis paniculata is used for the treatment of pharyngolaryngitis, diarrhoea, dysentery and cough with thick sputum, carbuncle, sores and snake bites. Various preparations and compound formulas of the herb have been used with significant effect rates to treat infectious and non-infectious diseases, described for conditions such as epidemic encephalitis B, suppurative otitis media, neonatal subcutaneous annular ulcer, vaginitis, cervical erosion, pelvic inflammation, herpes zoster, chicken pox, mumps, neurodermatitis, eczema, and burns. A primary use of Andrographis paniculata is for the prevention and treatment of the common cold. It appears to have antithrombotic actions, so it is beneficial in cardiovascular disease. Pharmacological and clinical studies suggest that it has potential to treat in diseases like cancer and HIV infections.

PHYTOCHEMICAL CONSTITUENTS-

Therapeutically active constituent of *Kalmegh* found in aerial parts. Andrographis paniculata contains diterpenes, lactones and flavonoids and polyphenols. [14] Flavonoids mainly exist in the root, but have also been isolated from the leaves. Aerial parts contain alkanes, ketones, and aldehydes and the bitter principles in the leaves were due to presence of the lactone andrographolide named kalmeghin. Andrographis paniculata has various compounds in its aerial parts and roots and these are often used in extracting its active principles. Diverse factors such as geographical region, harvest time and processing method account for the variability in Sits chemical content. [13, 14]

The primary active constituent of Andrographis paniculata is the Andrographolide. [15] It is colourless bitter in taste and crystalline and known as diterpenes lactone.

There are four lactones in Andrographis paniculata viz., (1) 14-deoxyandrographolide and (2) andrographolide, (3) neoandrographolide (a non-bitter, C 3 O glucoside derivative of the major constituent andrographolide) and (4) 14-deoxy-11,12-di-dehydro-andrographolide. Other compounds include 14-deoxy-11-oxoandrographolide, di-dehydro andrographolide/andrographolide D, 14deoxyandrographolide, non-bitter compound is neo andrographolide, homoandrographolide, andrographosterin, andrograpanin, α sitosterol, stigma sterol. Apigenin-7, 4-dio-methyl ether, 5hydroxy 7, 8, 2, 3-tetramethoxy flavones, monohydroxy tri-methyl flavones, andrographin, dihydroxy di-methoxy flavoue, panicolin, andrographoneo, andrographoside, andropani-culoside an andrograpanin, Isoandrographolide and skollcaflavone (912). Six ent-labdene diterpenoid i.e. 3-o-beta-Dglucopyranosyl-14, 19dideoxyandrographolide, 14-deox, 17hydroxyandrographolide, 19-o-[beta-D-apiofuranosy 1-2betaD-glucopyranoyl]-3, 14-dideoxyandiographolide, 3-obeta-Dglucopyranosyl-andro-grapholide, 12S-hydroxy andrographolide and andrographatoside. These compounds showed inhibitor activity against several fungal and bacterial strains. [16]

ANALYSIS OF PHYTOCHEMICAL CONSTITUENTS [17]-

Analysis of the plant for various phytochemical constituent present were carried out for different solvent ((hexane, chloroform, dichloromethane, ethyl acetate, acetone, methanol, water, ethanol and CO_2) extracts using standard methods.

Test for Carbohydrates-

Molisch's test was performed to detect carbohydrates. Few drops of alcoholic solution of alpha naphthol were added to the extracts. Then, added 1 ml of concentrated sulphuric acid along the sides of the test tube. Formation of violet ring at the junction of the liquids indicated the presence of carbohydrates.

Test for Alkaloids-

Crude extract was mixed with 2 ml of Wagner's reagent. Reddish brown colour precipitate indicated the presence of alkaloids.

Test for Coumarin -

Glycoside 10 %NaOH was added to the extract and few drops of chloroform was also added. Observation of yellow colour indicated the presence of coumarin.

Test for Saponins-

Foam test was performed to test the presence of saponins. To 2 ml of extract, added 6 ml of water in a test tube and was shaken vigorously. Formation of persistent foam confirmed the presence of saponins.

Test for Flavonoids-

Alkaline reagent test was performed to test the presence of flavonoids. Crude extract was mixed with 2 ml of 2% solution of NaOH. An intense yellow colour was formed which turned colourless on addition of few drops of diluted acid which indicated the presence of flavonoids.

Test for Phytosterols-

Salkowski test was used to detect phytosterols. To 2 ml of aqueous extract, 2ml of chloroform and 2 ml of concentrated H2SO4 was added. The solution was shaken well. As a result chloroform layer turned red and acid layer showed greenish yellow fluorescence.

Test for Phenols and Tannins-

Crude extract was mixed with 2 ml of 2% solution of FeCl3. A blue-green or black coloration indicated the presence of phenols and tannins.

Test for Proteins-

Ninhydrin test was employed to detect the presence of proteins. Crude extract when boiled with 2 ml of 0.2 % solution of ninhydrin, violet colour appeared suggesting the presence of amino acids and proteins.

Test for Terpenoids-

One ml of the extract was treated with Borsche's reagent (2, 4-dinitrophenyl hydrazine in methyl alcohol) and 1ml of 3M HCl. Formation of orange colour indicated the presence of terpenoids.

PHARMACOLOGICAL ACTIVITIES-

Hepatoprotective activity-

There were limited studies are available on the effects of crude extracts of *Andrographis paniculata* on liver functions. Most of the studies for hepatic effects have been conducted on either most active component present in Kalmegh viz., andrographolide or other active principles. [18] Singha et al reported that the protection against acetaminophen-induced reduction in volume and contents of bile was better due to andrographolide than that produced by silymarin. Multiple-dose pre-treatment with arabinogalactan proteins and andrographolide was protective than that of silymarin against ethanol induced hepatotoxicity in mice. [19] Choudhury and Poddar were reported that oral administration with an extract of *Andrographis paniculata* to the pre- and post-treatment of adult rats was protective against ethanol induced increase in serum transaminases. According to Choudhury et al, there was none effect on serum transaminases enzyme of normal adult rats in single and multiple doses for seven and 15 consecutive days feed with Andrographis extract [20] A comparative in vitro study on the effect of leaf extract and andrographolide on carbon tetrachloride (CCl_4)-induced hepatic microsomal lipid peroxidation revealed that lipid peroxidation was completely protected by the extract but not by andrographolide. This indicates the hepatoprotective effect is not only due to the presence of andrographolide. [20] Hepatoprotective effects of the crude alcohol extract of leaves against CCl_4-induced liver damage have also been reported by Rana and Avadhoot. [21] A. Handa and Sharma were comparatively proved the andrographolide, methanol extract of the whole plant containing equivalent amounts of andrographolide, and an andrographolide-free methanol extract against CCl_4-induced liver damage in rats. The CCl_4 induced increases in serum transaminases, serum alkaline phosphatase, serum bilirubin, and hepatic triglycerides were inhibited by 48.6-, 32- and 15 percent, for andrographolide, methanol extract, and andrographolide-free methanol extract, respectively. Since all three treatments resulted in improvement in liver

histology [22], a hepatoprotective role of *Andrographis paniculata* constituents other than andrographolide is suggested and corroborates the observation made by Choudhury and Poddar. [23] The CCl4-induced increase in pentobarbitone induced sleep time in mice is also completely normalized by andrographolide. The effects of intraperitoneal (i.p.) pre-treatment for three consecutive days with andrographolide on CCl4- or tert-butyl hydro peroxide-induced hepatotoxicity in mice were compared with two other diterpenes – andrographiside and neoandrographolide. Both compounds showed a greater protective effect than andrographolide. The protection by andrographiside and neoandrographolide was comparable to silymarin, and neoandrographolide normalized glutathione levels. [24] Trivedi et al were observed that reduced activities of hepatic antioxidant enzymes (superoxide dismutase, catalase, and glutathione peroxidase), depletion of hepatic glutathione, and increased activities of hepatic γ-glutamyl transpeptidase, glutathione-S-transferase, and lipid peroxidase caused by hexachlorocyclohexane in mice have been protected by both the crude extract of *Andrographis paniculata* and andrographolide. [25] Oral or i.p. pre-treatment with andrographolide was also protective against galactosamine-induced liver damage in rats and prevented changes in biochemical parameters and liver histology. Similar protection was observed when rats were treated with andrographolide post-acetaminophen challenge, [26, 27] and on an ex vivo preparation of isolated rat hepatocytes. [23]

Immuno-stimulatory activity-

Puri A was conducted an experiment that intragastric administration of an ethanol extract of the aerial parts (25mg/kg body weight) or purified andrographolides (1 mg/kg body weight) to mice stimulated antibody production and the delayed-type hypersensitivity response to sheep red blood cells. The extract also stimulated a non-specific immune response in mice, measured by macrophage migration index, phagocytosis of [14C] leucine-labelled E. coli, and proliferation of splenic lymphocytes. The extract was more effective than either andrographolide or neoandrographolide alone, suggesting that other constituents may be involved in the immuno-stimulant response. [28]

Antipyretic activity-

Intragastric administration of an ethanol extract of the aerial parts (500mg/kg body weight) decreased yeast-induced pyrexia in rats. [29] The extract was reported to be as effective as 200 mg/kg body weight of aspirin, and no toxicity was observed at doses up to 600 mg/kg body weight. [30] Intragastric administration of andrographolide (100 mg/kg body weight) to mice decreased brewer's yeast-induced pyrexia. [31] Intragastric administration of deoxyandrographolide, andrographolide, neoandrographolide or 11, 12-didehydro-14-deoxyandrographolide (100 mg/kg body weight) to mice, rats or rabbits reduced pyrexia induced by 2, 4-dinitrophenol or endotoxins. [32]

Antioxidant effects-

Verma N et al. has been proved the antioxidant effects of the aqueous extract on liver defense systems in lymphoma bearing mice. The aqueous extract and hydro alcoholic extract of the

Andrographis paniculata showed the increase in activities of enzymes like catalase, superoxide dismutase and glutathione-S transferase and reduced lactate dehydrogenase activity. The results performed with that of aqueous extract of A. paniculata exhibited a greater antioxidant activity than the ethanolic extract in all model systems tested. [33] Ojha SK et al. resulted that the hydro alcoholic extract of *Andrographis paniculata* possesses oxidative alterations in myocardium and confers substantial cardio protective activity by facilitating in retaining the cardiac function in a Norma manner. [34]

Hypotensive activity-

Andrographis paniculata is reported to have, by acting through β-adrenoceptors, autonomic ganglion receptor and angiotensin converting enzyme (ACE) inhibitory activity. [35] The 4th week of the extract treatment in SH rats significantly increases the relaxation responses to ACh as a result of possible improvement in the endothelial function; these are comparable with the study. Conversely the plant possesses a remarkable capability to challenge the norepinephrine induced contractions resulting in vaso relaxation in isolated rat. [36] The improvement in relaxation responses to ACh following chronic administration of chloroform extract is most likely due to the activation of NO synthesis and ultimate stimulation of NO production in endothelial cells. Moreover, the effects of chronic administration are evidently suggestive of increased responsiveness of the vascular smooth muscle to NO since 4week treatment with the extract was found to enhance the relaxation responses to the action of the endothelium independent vasodilator SNP. This was the comparative study between effects of chloroform extract *Andrographis paniculata* to the effects of Verapamil, which acts by blocking the L-type Ca^{2+} current and high K^{+} activated pathways to relax the smooth muscle. [37]

Antidiabetic activity-

Antidiabetic property of *Andrographis paniculata* was confirmed by Borhanuddin et al. and Husen et al. in aqueous extract [38-39] and by Zhang et al. in ethanolic extract. [40] Along with antihyperglycemic property, the ethanolic extract may also reduce oxidative stress in diabetic rats as studied by Zhang et al. [41] further, it was concluded by Yu BC et al. that the andrographolide was responsible for the antihyperglycemic activity. [42] Finally the antidiabetic potential of A. paniculata was found to restore impaired oestrous cycle in alloxan induced diabetic rats. [43]

Anti-inflammatory activity-

Andrographis paniculata at its optimal dosages can also inhibit the production of inflammatory mediators and alleviate acute hazards. [44] Shen et al. observed that the andrographolide, which is an active component of A. paniculata, inhibits inflammatory responses by rat Neutrophils. [45] It was also found to inhibit the tumour specific angiogenesis by regulating the production of various pro and anti-angiogenic factors by in vivo and in vitro studies. [46] In a study by Wang et al. A. paniculata was found to alleviate atherosclerotic artery stenosis induced by de-endothelialisation and high cholesterol diet as well as lower the restenosis rate after experimental angioplasty. [47] Further in a research by

Coon et al, it was safe and efficacious for the relief of symptoms of uncomplicated upper respiratory tract infection. [48]

Antibacterial activity-

An ethanol extract of the leaves inhibited the growth in vitro of Escherichia coli and Staphylococcus aureus1. A 50% methanol extract of the leaves inhibited growth in vitro of Proteus vulgaris. [49] However, no in vitro antibacterial activity was observed when dried powder from the aerial parts was tested against E. coli, Staphylococcus aureus, Salmonella typhi or Shigella species. [50]

Anti-plasmodial activity-

In vitro studies of Dua and his coworkers (2004)146 revealed that compound 1,2-dihydroxy- 6,8-dimethoxyxanthone possessed substantial anti-plasmodial activity against Plasmodium falciparum with its IC50 value of 4 µg ml−1. Xanthones bearing hydroxyl group at 2 positions demonstrated most potent activity while xanthones with hydroxyl group at 1, 4 or 8 position possessed very low activity. In vivo antimalarial sensitivity test of this compound on Swiss Albino mice with Plasmodium berghei infection using Peters' 4-day test gave substantial reduction (62%) in parasitaemia after treating the mice with 30 mg kg−1 dose84 The methanolic extract significantly inhibited Plasmodium falciparum at a 50-percent inhibitory concentration (IC50) of 7.2µg/mL. [51] One clinical trial has investigated the efficacy of a standardized A. paniculata extract to prevent the common cold by Caceres 107 healthy students in a rural school had daily taken either placebo or a dose of 200 mg (minimum 5.8%) of Kan Jang (a formulation of A. paniculata provided by the Swedish Herbal Institute) for three months. The number of colds occurring over a three month period was observed. After 1 month no significant difference was found. However, the difference was statistically significant in the second and third month. The placebo group was 2.1 times more likely to catcha cold than the Kan Jang group. The incidence of the common cold was 30% in the A. paniculata group, whereas the incidence was 62% in the placebo group. [52]

Antiviral activity-

Andrographolide, neoandrographolide and 14-deoxy11, 12-didehydroandrographolide are described to be viricidal activity against herpes simplex virus 1 (HSV-1) without having any significant cytotoxicity. [53]

Immuno-modulatory activity-

In 1993, Puri et al. reported that the ethanolic extract and purified diterpene andrographolides of Andrographis paniculata (Acanthaceae) induced significant stimulation of antibody and delayed type hypersensitivity (DTH) response to sheep red blood cells (SRBC) in mice. [54] While in 2005, Reddy et al. isolated six known compounds like andrographolide, 14-deoxy11,12-didehydroandrographolide, andrograpanin, 14-deoxyandrographolide, (+/-)-5-hydroxy-7,8dimethoxyflavanone, and 5-hydroxy-7,8-dimethoxyflavone and one Novel bis-andrographolide from the aerial parts of Andrographis paniculata and found that these compounds have positive results for the anti HIV and cytotoxic activity. [55] Panossian A et al (2002) has proved the immunomodulatory properties of a diterpene lactone andrographolide and a standardized

preparation (Coded name -Kan Jang) of Andrographis paniculata. Proliferation of peripheral blood lymphocytes (PBL) induced by phytohemagglutinin (PHA) was enhanced by co-stimulation with Andrographolide and Kan Jang. At the same study of Andrographolide and Kan Jang inhibit spontaneous proliferation of PBL. [56]

Cytotoxic activity-

Singh RP examined the chemo preventive potential of Hydro-alcoholic extract of Andrographis paniculata against chemo toxic effects including carcinogenicity on drug metabolizing enzymes, antioxidant enzymes, glutathione content, lactate dehydrogenase (LDH), and lipid peroxidation in the liver of Swiss albino mice. In the lung, SOD, catalase and DTD, in the kidney catalase, DTD and GST, and in the fore stomach SOD and DTD showed a significant increase at both dose levels of treatment. [57] Rajagopal et al. in 2003 has been suggested that the isolated compound andrographolide has an interesting pharmacophore with anticancer activity and immunomodulatory activities against B16F0 melanoma syngenic and HT-29 xenograft models. [58] Further, in 2004, Kumar et al screened the positive anticancer and immunomodulatory activity of the methanolic for human cancer and immune cells. [59] In 2005 Cheung et al. carried out the in vitro experiment and concluded that ethanolic extract of Andrographis paniculata and its main diterpenoid components has cytotoxicities in various cancer cells and concluded that it was significantly growth inhibitory to human acute myeloid leukemic HL- 60 cells with an IC (50) value of 14.01 µg/ml after 24 hours of treatment. [60] In 2005, Wiart et al. found that some isolated compounds, i.e. Andrographolide, neoandrographolide, and 14-deoxy-11,12- didehydroandrographolide, ent-labdene diterpenes showed viricidal effect against herpes simplex virus 1 (HSV-1). None of these compounds exhibited significant cytotoxicity at viricidal concentrations. [61] Further, aqueous extracts of A. paniculata are expected to be scorpion venom antidotes with low cytotoxicity. [62] An early enhancement of antibody-dependent complement mediated cytotoxicity of A. paniculata was also observed by Sheeja et al. in 2007 in normal as well as tumour-bearing animals. [63] In 2006 in an experimental studied by Zhou et al. and it was shown that the key mediators in relaying the cell death signaling initiated by Andrographolide was found to be proapoptotic Bcl-2. [64]

Antimalarial activity-

Chander R has concluded that 50% ethanolic extract of the aerial parts inhibited the growth of Plasmodium berghei both in vitro (100 mg/ml) and in mice after intragastric administration (1 g/kg body weight). [65] Intragastric administration of a 1-butanol, chloroform or ethanol–water extract of the aerial parts to Mastomys natalensis inhibited the growth of P. berghei at doses of 1–2 g/kg body weight. Bhaumik A et al reported that Andrographolide (5 mg/kg body weight) and neoandrographolide (2.5mg/kg body weight) were also effective when administered by gastric lavage. [66]

Anti-human immunodeficiency virus (HIV) activity-

Yao XJ has experimentally proved that aqueous extract of the leaves of Andrographis inhibited HIV-1 infection and replication in the lymphoid cell line MOLT-4. [67] Chang RS et al concluded that a hot aqueous extract of the aerial parts reduced the percentage of HIV antigen-positive H9 cells. [68] Chang RS reported that Dehydro andrographolide inhibited HIV-1 and HIV-1 (UCD123) infection of H9 cells at 1.6mg/ ml and 50mg/ml, respectively, and also inhibited HIV1 infection of human lymphocytes at 50mg/ml. [69] Otake T reported that a methanolic extract of the leaves suppressed syncytia formation in co-cultures of uninfected and HIV-1infected MOLT cells (median effective dose [ED50] 70mg/ml). [70]

Anti-Hyperglycaemic and Renal Protective Activities-

According to N .K. Rao, the chloroform extract of roots of *kalmegh* produced a dose-dependent hypoglycaemia in alloxan induced diabetic rats. It produced significant reduction in blood glucose with doses of 50, 100 and 150 mg/kg body weight respectively compared to control group. At the dose of 150 mg/kg the hypoglycemic effect was observed up to 24 hrs while glibenclamide produced maximum reduction of 50.44% (4 h, $p<0.01$) compared to control group. Chronic administration of *kalmegh* to alloxan induced diabetic rats for four weeks produced significant blood glucose reduction. Significant reduction was observed from the first week by both extract and glibenclamide at the doses of 150 mg/kg and 0.040 mg/kg. At the end of 4th week extract produced significant blood glucose reduction of 59.15% ($p<0.001$). On the other hand, glibenclamide produced significant blood glucose reduction of 62.02% ($p<0.001$). The activity of the extract (150 mg/kg) is not significantly different ($p<0.05$) from the standard drug glibenclamide (0.040 mg/kg). At the end of 4 weeks, major increase in urinary secretion of proteins, albumin and urea is observed in alloxan-induced diabetic rats. While no significant increase is observed in *Andrographis paniculata* extract (150 mg/kg) and glibenclamide (0.040 mg/kg) treated group of rats. [71]

CONCLUSION-

From the Kalmegh has been extensively used as traditional medicine in India, China and Southeast Asia. Different types of formulations, extracts and pure compounds obtained from this plant have been shown to possess biological activities including anti-microbial, anti-inflammatory, antioxidant, anti-diabetic, cytotoxicity, immune modulatory, sex hormone modulatory, liver enzyme modulatory, antimalaria, anti-angiogenic and hepato-renal protective activity.

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