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Evaluation of an emerging medicinal crop *Kalmegh* [*Andrographis paniculata* (Burm. F.) Wall. Ex. Nees] for commercial cultivation and pharmaceutical & industrial uses: A review

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Abstract
Kalmegh [*Andrographis paniculata* (Burm. f.) Wall. Ex. Nees] belonging to the family acanthaceae is one of the most important medicinal crops, indigenous to India and Sri Lanka. The fresh and dried leaves and juice extracted from the herb are official drugs in Indian pharmacopoeia and have been used in Indian systems of medicine since time immemorial. Looking at the utility and pharmacological importance of *Andrographis paniculata*, an overview is conducted considering some useful aspects like, origin and distribution, plant botany, taxonomy, genetics, edaphic and climatic requirements, methods of propagation, important varieties, planting geometry, nutrient management, irrigation management, insect-pest, diseases and weed management, maturity and harvesting period, therapeutic uses, phyto-chemistry and phamacognosical studies to initiate systematic and commercial cultivation of *kalmegh* for industrial uses.

Keywords: *Kalmegh*, medicinal, cultivation, industry, pharmacology, diseases

1. Introduction
Plants for the purpose of medicine have been used since ancient times to heal and cure diseases and to improve the health of human beings. According to the World Health Organization (WHO), the goal of "Health for All" can't be achieved without herbal medicines. India exports herbal materials and medicines to the tune of nearly 600 crores annually. About 960 species of medicinal plants are estimated to be in trade of which 178 species have annual consumption levels in excess of 100 metric tones (Planning Commission, 2011) [53]. Among various medicinal plants, there is a great demand of *kalmegh* in the country as well as in abroad. *Kalmegh* is one of the most important *kharif* seasonal medicinal plants which is a boon for weaker section of rural areas and plays an important role for their income generation. The Indian National Medicinal Plants Board has proposed 32 prioritized medicinal plant list, among them *kalmegh* is at 17th position. It has an important place in India pharmacopoeia and is being prominently used in 26 ayurvedic formulae.
It is known for its preventive and curative properties (Farooqi and Sreeram, 2010) [14]**.** as whole plant is used in drugs (stem, leaves and inflorescence) which is the source of several diterpenoids of which andrographolide is important one (Aparna and Bagyaraj, 2007) [3]**.** Recent experiments have also shown its antityphoid and antibiotic activity (Purohit and Vyas, 2005). The leaves and aerial parts of plant are used in treatment of fever, liver disease, diabetes, snake bite, jaundice, dysentery, chronic malaria and sore throat (Shankar *et al.*, 2012 and Sanjhuta *et al.*, 2008**)** [68, 65]**.** In India also, the entire plant is used to obtain andrographolide, the most important pharmacologically active compound **(**Randa and Sharma, 1990) [59]. Having such a medicinal value and broad geographical distribution of this plant throughout the country, its indiscriminate collection from wild sources without paying any attention towards its conservation and domestication in regular agriculture has caused a sharp decline in the availability of drug to the industries and escalation in its prices. Therefore the heavy demand of phytochemicals especially diterpene lactone like andrographolide in India as well as international markets has motivated Indian farmers to take up commercial cultivation of *kalmegh*.

2. Geography, ecology and biology
2.1 Origin and distribution
Kalmegh is native to Taiwan, mainland, China, India and Sri Lanka. It is commonly found in the tropical and subtropical Asia, Southeast Asia, and some other countries including Cambodia, Caribbean islands, Indonesia Laos, Malaysia, Myanmar, Sri Lanka, Thailand and

2.2 Taxonomy

Andrographis paniculata one of the most important medicinal crop, belonging to the family Acanthaceae and order personales (table: 1). A total number of species of this crop varied in different reports, which comprises either 19 (USDA 2014) [81]. 28 (Parixit *et al*., 2012; Valdiani *et al*., 2012) [51, 82]. 40 (Mishra *et al.,* 2007; Sharma and Sharma 2013) [42], or 44 (Borhanuddin *et al.,* 1993) [7] species. However the genus *Andrographis* consists of 40 species and about 19 species are reported to be available in India, out of which *Andrographis paniculata* and *Andrographis alata* have medicinal properties. The exact numbers of species of *Andrographis* genus are not validated yet. Total number of chromosomes of *Andrographis Paniculata* is 25 and 50 in gametophytic (Madav *et al*., 1995 [37] and sporophytic (Sheeja *et al.,* 2007) [71]. count, respectively. In addition, genotypic differences are important considerations to find out high yielding germplasms of *kalmegh* for enhancing productivity and profitability.

Table 1: Taxonomic classification

Domain	Eukaryotic
Kingdom	Plantae
Subkingdom	Tracheobionta
Division	Angiosperm
Class	Dicotyledonae
Subclass	Gamopellatae
Series	Bicarpellatae
Order	Personales
Family	Acanthaceae
Subfamily	Acanthoideae
Tribe	Justiciae
Subtribe	Andrographideae
Genus	*Andrographis*
Species	*Andrographis paniculata* (Burm. f.) Wall ex. Nees

Reddy *et al.,* 2005; She *et al*., 2008; Sheeja and Kuttan 2007) [61].

1.2.1 Synonyms

Kalmegh is well known under different vernacular names such as Kirta, Kiryata, Kalpnath, Create, Green Chirata and King of Bitters. It is also called as maha-tita or bhui-neem because of its similarity in appearance and bitter taste as that of neem (*Azadirachta indica* A. Juss). However, there are different names of *kalmegh* according to different languages are presented in the table: 2 as written under:

Table 2: Different names of *kalmegh*

Arab	Quasabhuva
Bengali	Kalmegh
English	The Creat, King of bitters
Gujarati	Kariyatu
Hindi	Kirayat
Kannad	Nelaberu
Malayalam	Kiriyattu
Oriya	bhuinimo
Marathi	Oli-kiryata, Oriya
Sanskrit	Kalmegha
Tamil	Nilavembu
Telugu	Nilavembu

2.3 Plant Botany

Kalmegh is an annual, branched, herbaceous plant growing to a height of 30– 110 cm in moist and shady places having stem acutely quadrangular, slender, much branched, easily broken fragile texture which is dark green in colour, squared in cross-section with longitudinal furrows and wings along the angles.

The leaves are simple, opposite, lanceolate, glabrous, lance-shaped, 2–12 cm long, and 1–3 cm wide with hairless blades measuring up to 8 centimeters long by 2.5 wide. Margin of the leaves are acute and entire or slightly undulated and upper leaves often bract form with short petiole (Table: 3).

The flowers are small in size, borne in spreading racemes which possess botanical features of calyx 5-particle, small, linear; corolla tube narrow, about 6 mm long; limb longer than the tube, bilabiate; upper lip oblong, white with a yellowish top; lower lip broadly cuneate, 3-lobed, white with violet markings; stamens 2, inserted in the throat and far exserted; anther basally bearded. Superior ovary, 2-celled; style far exerted. The fruit of the plant is a capsule which is erect, linear-oblong, 1–2 cm long and 2–5 mm wide, compressed, longitudinally furrowed on broad faces, acute at both ends, thinly glandular-hairy which contains many yellow brown seeds which are very small in size and sub quadrate (Kumar *et al*., 2012) [79] . Inflorescence of the plant is characterized as patent, terminal and axillary in panicle, 10–30 mm long; bract small; pedicel short.

Table: 3 Botanical description of *kalmegh*

Traits	Values/characteristics
Plant height	30-110 cm
Stem	Dark green
Length	30-100 cm
Diameter	2-6 mm
Shape	Quadrangular with longitudinal furrows and wings on the angles of the young parts, slightly enlarged at the nodes
leaves	Glabrous
length	2-12 cm
width	1-3 cm
Arrangement	Lanceolate
Shape	Pinnate, acute apex, entire margin
flowers	White with rose-purple spots on the petals
Size	Small, in lax spreading axillary and terminal racemes or panicles
Seed capsule	linear-oblong, acute at both ends
Size	1.9 cm × 0.3 cm
color	Yellowish brown
Shape	Subquadrate, numerous

Fig 1: Flower of *kalmegh*

Fig 2: Leaves of *kalmegh*

Fig 3: Seeds of *kalmegh*

2.4 Genetical aspects

Total number of chromosomes in *kalmegh* are 2n = 50. Lattoo *et al*., 2006, induced genetic male sterility (6.0 to 14.0 %) in *A. paniculata* at M-1 following 20 KR gamma irradiation and the male sterile gene was found to be monogenic recessive to normal. The male sterile gene acted upon the tapetal layer and also affected non sporogenous tissue within the anther locule resulting in encroachment of the locule and thereby, significantly reducing the pollen production and enhancing the formation of abortive pollen. However, female fertility remained unimpaired and fully intact in this plant.

2.5 Climatic requirement

The climatic requirement of the plant is hot and humid conditions with ample sunshine can be grown in hedge rows throughout the plane lands, hill slopes, waste ground, farms, moist habitat zones, seashores, and roadsides. However it is found naturally in the humid and hot places, sometime it is also available in dry forest. For the cultivation point of view tropical climate is good for it except the temperate climate of cold region. Its cultivation can also be taken on moist shady places, forests area, and wastelands which are suitable and preferable for its vegetative growth and development (Parixit *et al*., 2012; Reddy *et al*., 2005) [51, 61]. Flowering and fruiting continues up to December until temperature drops drastically in Northern plains.

2.6 Edaphic requirement

Kalmegh is a hard plant which can be grown in all types of the normal soils which explains its wide distribution. It grows in the soil types where almost no other plant can be cultivated, particularly serpentine soil, which is relatively higher in heavy metals like Al, Cu and Zn. (Samantaray *et al.*, 2001) [64]. However it shows good growth and development especially in light black soil, sandy loam soil with rich organic content or can be cultivated on a wide range of soils from loam to lateritic with moderate fertility level. The soil which are favorable for growth of Chilli and Cotton, are good for *Kalmegh* cultivation. For the good production point of view, stagnation of water or water logging should not be in the field or the soil which is flooded or wet throughout the year may be avoided for its cultivation. (Kasetklangklung, 1996) [29]. The pH of soil must be in the range of 6.5 -8.5.

3. Agronomic cultivation

3.1 Propagation

Generally propagation of *kalmegh* is through shattered seeds in nature. *Kalmegh* can be cultivated by the genetic method (seeds) as well as vegetative method (layering/ Cutting). However, vegetative propagation is also suitable in certain special cases through layering as each node is capable of producing enough roots and seeds are small and may remain dormant for five to six months. But from the commercial cultivation point of view, the genetic propagation (by using seeds) is good as it is also very easy to propagate the crop by seeds. This can be done by using two methods, direct seeding and transplanting. For transplanting, nursery can be raised and maintained for the better results and germination percentage.

3.1.1 Direct seeding

Direct seeding is the method comes under genetic propagation in which farmer broadcasts the seeds of *kalmegh* directly in the field. The germination percentage may be good by this way but there may be problem of the weed infestation in the field as initial growth of the plant is very slow and lack of competitive advantages against weed population as devoid of transplantation of 40-45 days old seedlings in the main field. So for the commercial point of view, nursery raising is better than direct seedling.

3.1.2 Nursery Management and transplanting

For raising crop in one hectare, three beds of 10 m × 2 m size should be tilled, pulverized and leveled during the month of May. About 650-750 gm seeds are required for raising nursery for one hectare of land. The nursery beds cab be prepared manually with the help of spade and pulverized thoroughly with a hoe. Thereafter, stones and pebbles present in the soil are removed. Liberal use of organic manure like farm yard manures, vermicomost in the nursery is advised for raising healthy seedling with good vigour. Seeds should be covered by very thin layer of soil and compost mixture. After pulverizing and leveling the bed surface seeds can be sown in the shallow furrows prepared at the distance of 5- 6 cm,

having the depth of 1.5 cm to facilitate quick seeds germination and emergence of seedlings by proper aeration and restrict crust formation. The uniform layer of straw mulch can also be used to maintain soil moisture and temperature and increasing the rate of seeds germination. The irrigations are provided as per need (usually in morning hours) with the help of water can. Just after germination of the seeds within 6-7 days, the layer of straw mulch should be removed immediately.

Approximately 40-45 days (1.5 months) old seedlings are uprooted from the nursery by holding them at the base and pulling one by one unlike the conventional method of transplanting. Seedlings should be uprooted carefully with a good amount of nursery- bed soil attached to roots and without any injury either to the root or shoot 30 minutes at the most before transplanting. Within 10-15 minutes of uprooting, seedlings of *kalmegh* are transplanted with the help of *khurpi* by making a hole and using index finger and thumb and gently pressing the base of the seedling into the thoroughly pulverized soil at the intersection of the markings. Immediately, after transplanting of seedlings in the main field, a light irrigation should be given to avoid moisture stress and promote the fast initiation of establishment process of the young seedlings. Gap filling of seedlings can be done a week after transplanting by using the seedlings of nearly equal vigor from the same nursery to maintain optimum plant population.

Fig 4: *Kalmegh* nursery

Fig 5: Seedlings ready for transplanting

3.2 Important varieties

There are very limited varieties of *kalmegh* released, however, plant Breeder, Dr. H. O. Mishra from CIMAP, Lucknow developed and released a variety named CIM-Megha during 1980 which is one of the most important varieties of *kalmegh* being used for cultivation in northern India. Some of the other important varieties released for commercial cultivation are as under:

- AK-1 (Anand Kalmegh-1)
- IC-111286
- IC-111287
- IC-111289
- KI- 5
- IIIM (J)- 90

3.3 Plant geometry and spacing

Ram *et al.* (2008) [65]. in an experiment on effect of plant spacing on growth and herbage yield of *kalmegh*, observed that the maximum growth attributes *viz.*, plant spread, number of primary and secondary branches and number of leaves per plant was found at wider spacing (30 × 40 cm) and maximum fresh and dry herbage yield (94.18 q/ha and 54.33 q/ha) was obtained at closer spacing (30 × 30cm) and was concluded that planting at closer spacing (30 × 30 cm) was found optimum.

Makwana *et al.* (2010) [38]. also studied different plant spacing on yield of *kalmegh*- panchang under middle Gujarat conditions and observed that the growth attributes such as plant height (71.36 cm) and plant breadth (23.89 cm) at harvest stage were significantly higher when planted under 30 cm × 45 cm row to row and plant to plant spacings.. They also recorded the highest fresh herbage yield (10335 kg/ha) and dry herbage yield (4375 kg/ha) of *kalmegh* under plant geometry of 30 cm × 45 cm.

Kanjilal *et al.* (2002) [27]. in a study in Assam, India reported that higher yield of *A. paniculata* was found when planted in the first week of May with Crop spacing of 30 × 30 cm. Kumar *et al.* (2006) [32]. also studied the potential of *kalmegh* under North Indian conditions and concluded that the quality parameters; andrographolide content and its yield were found maximum at 135 DAT however, iron content was maximum at 120 DAS with 20 ×10 cm plant spacing. Singh *et al.* (2011) studied growth, behaviour, bio mass and diterpenoid lactones production in *kalmegh* strains at different population densities. They observed that planting at a closer spacing of 30 × 15 cm accommodating 222222 plants per hectare produced maximum dry biomass and andrographolide and neoandrographolide yield under the subtropical climate of North India.

Fig 6: Transplanting of *kalmegh* seedlings

Fig 7: Plant geometry of *kalmegh*

3.4 Nutrient Management

The growth and development of *kalmegh* is dependent on the soil condition and climatic factors like temperature, humidity, intensity and duration of radiant energy. The soil provides mineral nutrients and moisture, while the carbon dioxide of the atmosphere is utilized for photosynthesis. Under certain soil and climatic conditions, nutrients are not readily available to the crop in optimum amount and proportion. Under these circumstances, application of nutrients through organic and inorganic sources enhances the growth and yield attributes of *kalmegh*. Mineral fertilizers can be used to provide soil nutrients in order to maintain optimum soil fertility conditions and healthy growth of plants and quality yield. Chemical fertilizers help the growing crops to withstand stress conditions and in some cases these were used to correct plant nutrients deficiencies. According to Leonard (1986) [36], maximum net returns in crop production can adequately be sustained with adequate fertilizer program that will supply the amounts of plants nutrients needed. Similar type of observation was reported by Akinrinde (2006) [1]. in various crop production studies. According to Hue (1995) [22]. inadequate P supply will result in a decreased synthesis of RNA, the protein maker, leading to decreased growth. Grain yield is often severally reduced with P deficiency also (Jones *et al*., 2003) [24]. Potassium is required in least amount but in soil it is required in large amount by many crops and it is important for maintaining the osmotic potential and rigidity of plant cells; hence it plays a vital role in water relations in the plant.

Verma *et al*., (2018) [84]. conducted an experiment at Medicinal Plants Research and Development Center (MRDC), Pantnagar to study the effect of organic manures and different doses of nitrogen with same P_2O_5 and K_2O per hectare on growth attributes of *kalmegh* and concluded that application of vermicompost @ 5 t/ha and 75 kg nitrogen in two splits (37.5 kg N as basal application and 37.5 kg N as top dressing at 25 DAT) significantly achieved higher growth attributes like plant height, number of leaves and branches per plant and dry matter accumulation per meter square. Vijaya and seethalakshami. (2011) [85]. also studied the effect of vermicompost on the growth of *Andrographis paniculata*. Results shown that, significant plant growth was attained when the same vermicompost was amended with garden soil. Shahjahan *et al*. (2013) [67]. also reported that application of vermicompost gives significant increase in number of leaves per plant in *kalmegh***.** Application of vermicompost @ 2.5 t/ha along with inorganic fertilizers resulted in higher plant height, herbage and oil yield (70.2 cm, 11.98 t/ha and 31.61 kg/ha, respectively) in sweet basil (Munnusingh and Ramesh, 2002). Chauhan *et al*. (2002) [11]. And Haque *et al*. (2007) [19]. reported that the fresh herbage yield of *kalmegh* was increased with the increased application of vermicompost levels and the maximum yield was recorded with application of vermicompost @ 7.5 t/ha which might be attributed due to the increased photosynthesis and improved vegetative growth as a result of increased supply of nitrogen coming from decomposition of vermicompost. Tiwari *et al*. (2012) studied that organic sources of N @ 60 kg/ha applied through FYM produced maximum growth, fresh & dry herbage yield (37.12 and 25.59 q/ha), andrographolide content (2.55 %) and its yield (93.16 kg/ha) with the highest net income (Rs.1.2 lakh/ha). This was equally followed by vermicompost, poultry manure and urban compost each applied @ 60 kg N/ha. Hemalatha and Suresh (2012) [20]. observed that reason for increase in dry herbage yield of *kalmegh* under application of vermicompost is due to increase in fresh yield of herbage and also the integrated way has resulted in synergistic effect and encouraged the various growth attributes which ultimately helped in better absorption and utilization of nutrients by the plants, resulted in higher dry matter accumulation and their translocation to different plant parts which in turn reflected in better fresh herbage yield which directly helps in increased dry yield. Mishra *et al*. (2013) observed that there is significant variation in andrographolide content at different stages of life cycle of plant after 45 DAS, 75 DAS, 105 DAS and 135 DAS. Maximum increase in per cent andrographolide was observed 0.749 %, 0.764 %, 0.834 % and 0.893 % in plants treated with vermicompost + bio-fertilizer + chemical fertilizer in combination at an interval of 30 days. Thus integrated nutrient management along with vermicompost can be an alternative to chemical fertilizers for sustainable quality crops.

Hemalatha and Suresh, 2012 [20]]. studied the effect of organic, inorganic and bio fertilizers on growth and yield of *Kalmegh* at Horticultural College and Research Institute, Periyakulam. and reported that the highest plant height (56.54 cm /plant), number of branches (22.65 /plant) and number of leaves (41.40 /plant), leaf area (128.34 cm /plant), dry biomass (2.639 t/ha) and fresh herbage (1392.22 kg/ ha) and alkaloid yield (0.739 %) yields were recorded in the plots treated with FYM @ 15 t/ha along with 45: 25: 25 kg N, P_2O_5 and K_2O per hectare and 1 kg Azospirillum per hectare. Application of FYM @ 15 t/h along with N, P_2O_5 and K_2O @ 75: 75: 50 kg/ha + Panchagavya @ 3 % foliar spray recorded the highest growth parameters, nutrient uptake, yield and and rographoloid content followed by FYM @ 15 t/h along with Panchagavya @ 3 % only (Sanjutha *et al*, 2008) [65].

Ramesh *et al*. (2011) in a field experiment observed that poultry manures applied @ 2.63 t/ha along with 150 % recommended dosage of fertilizers, resulted in higher growth parameters in terms of plant height (42 cm), number of leaves (107.8), number of branches (124.6), leaf area (102 cm^2), plant spread (1131.4 cm^2), fresh leaf weight (12.4 gm), and herb yield (2.7 t/ha) of *kalmegh* (*Andrographis paniculata).* Detpiratmongkol *et al*. (2014) [13]. also reported that in *kalmegh*, application of poultry manure gave the highest leaf area index (LAI), total dry weight of plant and dry weight yield followed by pig manure, while cow manure gave the lowest. However application of 12.5 t/ha of poultry manure resulted in a significantly higher performance of growth

parameters, total dry weight and dry weight yield when compared to 2.5, 5, 7.5 and 10 t/ha, respectively.

Hemalatha and Suresh (2012) [20]. studied impact of integrated nutrients on growth and yield of *kalmegh*. They observed the highest plant height (56.54 cm), No. of branches (22.65) and No. of leaves (41.40), leaf area (128.34 cm^2), dry biomass (2.639 t/ha) and fresh herbage (1392.22 kg/ha) and alkaloid yield (0.739 %) of *Andrographis paniculata* were recorded in the treatment containing 45: 25: 25 kg N, P_2O_5 & K_2O per hectare + Azospirillum @ 1 kg/ha. However, Patel *et al.*, 2012 observed that effect of organic manures was found non-significant for growth parameters, yield and quality of *kalmegh* but slight improvements in chemical properties were observed due to continuous application of organic manures under study.

3.5 Irrigation management

After transplanting of seedlings, up to 8-10 days, a light irrigation as per requirement can be provided at a regular interval to facilitate the early establishment of seedlings. Afterward, there would be enough *mansoon* rainfall but the crop is irrigated as per soil moisture conditions of the field. In general there is no need of extra irrigation as the crop is transplanted in the season of monsoon. If it is not raining on the time the field can be irrigated at the interval of 20-25 days as per the requirement of the soil. The excess moisture during *mansoon* days should be drained out to avoid injury to the crop and to facilitate enhanced growth.

Fig 8: Irrigation by water can immediately after transplanting of *kalmegh* seedlings

Fig 9: Irrigation by channel

3.6 Application of growth regulators

Kumari *et al.*, 2017 [34]. conducted an experiment to study the effects of plant growth regulators on yield and andrographolide content of *kalmegh* (*Andrographis paniculata* Nees). Treatments were consisting of growth regulators NAA (40, 50 and 60 ppm), GA_3 (25, 50 and 100 ppm) and Paclobutrazol (100, 150 and 200 ppm) and distilled water spray as control. They concluded that application of paclobutrazol @ 100 ppm significantly increased the fresh and dry herbage weight, stem and their total. The foliar application of NAA @ 50 ppm was found very effective and recorded maximum cumulative dry herb yield, drying percentage and total andrographolide yield (3662 kg/ ha, 54.5 % and 58.89 kg/ ha respectively). The result obtained has clearly showed that *kalmegh* positively responded to NAA application.

3.7 Weed Management

Kalmegh is a short duration crop and grown in *kharif* season thus weed infestation is a big problem which deteriorate the quality and quantity of *kalmegh* herbs. So adoption of efficient weed management techniques can improve the growth attributes and increase leaf area index, crop growth rate, relative growth rate and herbage yield of plant. Predominant weeds associated with *kalmegh* are presented in table: 4.

Meena *et al.*, 2017 [40]. in an experimental study has reported that application of Pendimethalin @ 1 kg a.i. /ha as pre emergence followed by Quizalofop ethyl @ 50 g a.i. /ha as post emergence followed by one mechanical weeding can be taken as an alternative to the hand weeding for efficient weed control and achieving high biomass yield of *kalmegh* during *kharif* season. However hand weeding is best way of weed control if availability of labour.

Semwal *et al*, 2016 [66]. also reported that pre emergence application of pendimethalin 30 E.C.@ 1.0 kg a.i./ha along with post emergence application of quizalofop ethyl 5 E.C. @ 50 g a.i./ha at 3-5 leaves stage of weeds followed by mechanical weeding by hand hoe at 30- 35 DAT and pendimethalin 30 E.C. PE @1.0 kg a.i./ha followed by mechanical weeding by hand hoe at 30-35 DAT proved effective to increase plant height, number of branches, plant spread, leaf area index, plant dry weight/m^2 and dry herbage yield q/ha of *Kalmegh* (*Andrographis paniculata* Nees).

Table: 4 Predominant weeds associated with *kalmegh*

Type	Botanical Name	Common Name	Family	picture
Sedge	*Cyperus rotundus*	Motha/Nutsedge	Cyperaceae	
	Cyperus iria	Motha/Nutsedge	Cyperaceae	
	Cyperus diformis	Motha/Nutsedge	Cyperaceae	
Grasses	*Echinochloa crusgalli*	Sewai	Poaceae	
	Echinochloa colonum	Dawra	Poaceae	
	Cynodon dactylon	Doobghas	Poaceae	
	Eleusine indica	Goose grass	Poaceae	
	Panicum spp	Witch grass	Poaceae	
Broad leaf	*Ammania baccifera*	Ammania	Lythraceae	
	Acalypha indica	Indian copper leaf	Euphorbiaceae	

	Amaranthus virdis	Amaranth	Amaranthaceae	
	Phylanthus niruri	Hajardana	Euphorbiaceae	

Upadhyay *et al*, 2011 [42].

3.8 Insect-pest and diseases and their management

No major insect-pest and disease infestation has been reported in *kalmegh.* However, Rani and Sridhar (2005) [60]. conducted a survey during 2001 to 2002 in Bangalore, Karnataka to record various pests and their seasonal incidence on *Kalmegh*. Observations on pest incidence and plant parts attacked were recorded from 5 randomly selected beds (5 plants per bed) at 15 days interval. Brown Scale, *Parasaisettia nigra*, was found causing significant damage, as the affected plants exhibited stunted growth and drying, followed by semilooper, Panilla albopenstata which damaged the plants by feeding on young leaves, flowers buds and tender pods. This was thought to be first record of arthropod pests on *Kalmegh* from India. The nursery sandalwood seedlings were mainly attacked by six species of defoliators and two species of sap sucking insects (Ramadevi *et al*, 2005) [62].

Suganthy and Sakthivel (2013) [77] reported the effectiveness of aqueous leaf extract of *Azadirachtin* @ 1% or 2% upon *Andrographis paniculata* containing the insect pest population and also conserved more number of natural enemies like predatory coccinellids in S. nigrum. Growing cowpea as a border crop to conserve the coccinellid predators and marigold for the management of root-knot nematodes is recommended.

3.9 Maturity period and harvesting

Parashar *et al*. (2011) studied morpho-physiological evaluation of *Andrographis paniculata* at different growth stages. They found that, growth analytical parameter as well as morpho-physiological (*viz*., plant height, no. of leaves, no. of branches, crop fresh weight, crop dry weight, leaves fresh and dry weight, and herbage yield) parameters and specific leaf area increases up to 90 DAT and there after it gradually decline up to 120 DAP indicating the maturity of crop.

In general after the 2.5 - 3 months of transplanting, the crops start flowering, which are light white in colour. The pods start to form like the pod of rice plant. Slowly and slowly the pods start to mature. This is best indication to uproot the plant. The leaves of plant start dropping from top and the biomass remain same at the lower side of the plant. This is indication of harvesting. Generally this situation comes in the month of October and November. The plant is dried after the uprooting. If the farmer is interested in seed collection, the farmer can wait for one to two months. When most of pods mature fully in the month of January and February in this type farmer will get less leaves but he will get the income from the seeds.

The planting and harvesting time of this crop are considered to be very important for crop yield and quality. The active principle of a plant varies with time interval, different environmental conditions (Kumar *et al*., 2002) [30]. and time of harvesting had a major influence on productivity and quality of *Kalmegh* (Nemade *et al*., 2001) [47]**.** As per the earlier reports, the quality of *Kalmegh* decreases with the delay in harvesting (National Research Centre for Medicinal and Aromatic Plants, 2001) [46]. Therefore, a proper planting distance and an optimum harvest time need to be standardized for this crop.

The best harvesting period of *kalmegh* is at 3-5 months old or at 50 % blossom whereupon the highest quantity of andrographolide content is found. Wankhade *et al*., 2005 [88]. reported the planting time of 1st July and harvesting on 1st November for maximum herbage yield. However andrographolide content and yield was maximum with 1st July planting and 16th November harvesting. The maximum herbage yield was also reported by Faizabad centre with the planting and harvesting dates of 15th July and 16th November, respectively (Anonymous, 2002) [2]. The results revealed that the planting time on 1st July and harvesting between 1st to 16th November was suitable for obtaining higher herbage yield and total yield of Andrographolide and Iron.

Another study was also carried out at CCS Haryana Agricultural University, Hisar, India in the year 2005 and 2006 to investigate the influence of four harvesting times (120, 135, 150 DAT and at seed maturity) on growth, dry herbage biomass, seed yield and quality traits of *Andrographis paniculata.* The maximum values for dry herbage biomass yield (5.14 t /ha), andrographolide content (2.63 %) and total andrographolide yield (135.00 kg/ ha) were found when harvested at 135 DAT. However, the maximum iron content was estimated at 120 DAT. (Kumar and Kumar, 2013) [33]. Both growing region and seasonal changes have a strong impact on formation of the diterpene lactones in the plant. The highest concentration of the active components is found just before the plant blooms, making early fall the best time to harvest.

3.10 Storage

After harvesting of the plant materials, it is cleaned and after cutting in to different pieces, dried in hot air oven at 46 ºC - 50 ºC for 8 hours or until properly dried. The dried materials of the herbs then stored in air less polythene bags and kept in the cool places. (Tipakorn, 2002) [78].

4. Pharmaceutical aspects

4.1 Secondary metabolites

The characteristic secondary metabolites found in the *kalmegh* plant have considerably enhanced its pharmacological importance. A number of diterpenoids and diterpenoid glycosides of similar carbon skeleton have been isolated from *Andrographis* mainly the bitterest compounds

among them are andrographolide, neoandrographolide, deoxyandrographolide (Table: 5). Other such phytochemicals amassed by the plant are 14-deoxyandrographolide, 14-deoxy-11, 12-didehydroandrographolide, and rographiside, deoxyandrographiside, homoandrographolide, and rographan, and rographon, andro-graphosterin and stigmasterol (Siripong *et al.*, 1992) [76]. The leaves of *kalmegh* contain the highest amount of andrographolide (2.39%), the most important medicinally active phytochemical in the plant, while the seeds contain the lowest (Sharma *et al.*, 1992) [69]. Andrographolide has highly bitter in taste, colorless crystalline in appearance, and possess a "lactone function".

A variety of lab level methodologies are used to ensure a standardized level of and rographolides *viz*., thin-layer chromatography (TLC), ultraviolet spectrophotometry, liquid chromatography, and volumetric and colorimetric techniques. However HPLC among them are most robust and reliable for quantitative and qualitative profiles of and rographolides. For extraction of and rographolides, a solvent extraction method is usually employed using ethanol, and liquid extracts are the most common form of dispensing the product. Varied methodologies for isolation and extraction of and rographolides from the plant have been adopted by different working groups. In general, extraction of and rographolides is aqueous or aqueous methanolic and the extract is further fractionated with methanol-chloroform, dichloromethane and/or petroleum ether or hexane in accordance with the andrographolide fractions/moieties desired to be enriched for specific application. Usually aqueous or little amount of ethanol/methanol is used to isolate and rographolides for pharmacological investigations. To advance, solid–liquid extraction of stem and leaves of *Andrographis paniculata* is in precisely defined relative proportions of water and ethanol in order to obtain andrographolide (Wongkittipong *el at.*, 2004) [89].

The structure of andrographolide comprises

1. One a-alkylidene c-butyrolactone moiety,
2. Two olefin bonds Delta $^{8(17)}$ and Delta $^{12(13)}$ and
3. Three hydroxyls at C-3, C-19, and C-14. (Of the three hydroxyl groups, the one at C-14 is allylic in nature, and the others at C-3 and C-19 are secondary and primary, respectively).

Analysis of the whole plant, in a study (Matsuda *el al.*, 1994) [39] has given the following lactones in *kalmegh*

Table 5: Phytochemicals found in *kalmegh*

Comound	Chemical formula	Melting point
andrographolide	$C_{20}H_{30}O_5$	230-239 °C
14-deoxy-11- oxoandrographolide	$C_{20}H_{28}O_5$	98-100 °C
14- deoxy-11, 12-didehydroandrographolide	$C_{20}H_{30}O_4$	203- 204 °C
14-deoxyandrographolide	$C_{20}H_{30}O_4$	175 °C
neoandrographolide	$C_{26}H_{40}O_8$	167-168 °C

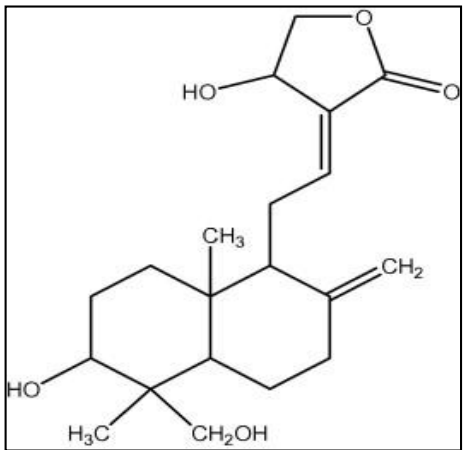

Fig 10: Andrographolide

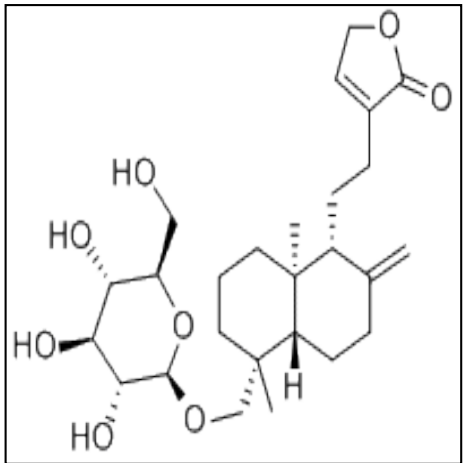

Fig 11: Neoandrographolide

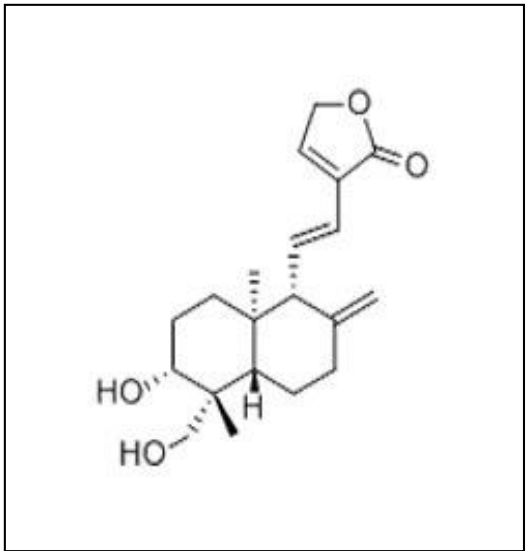

Fig 12: 14- Deoxy andrographolide

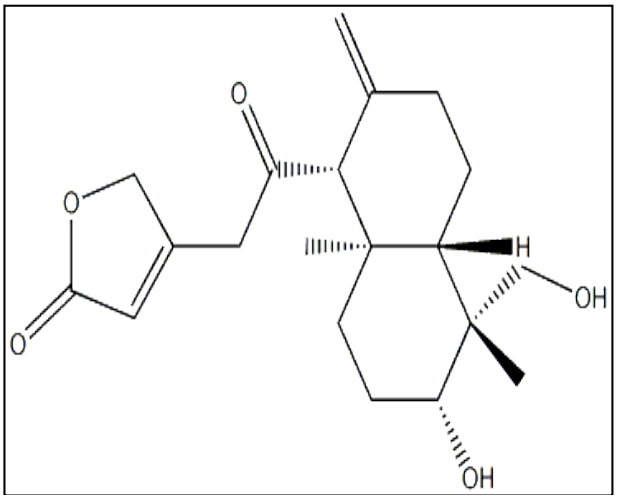

Fig 13: 14-deoxy-11- oxo andrographolide

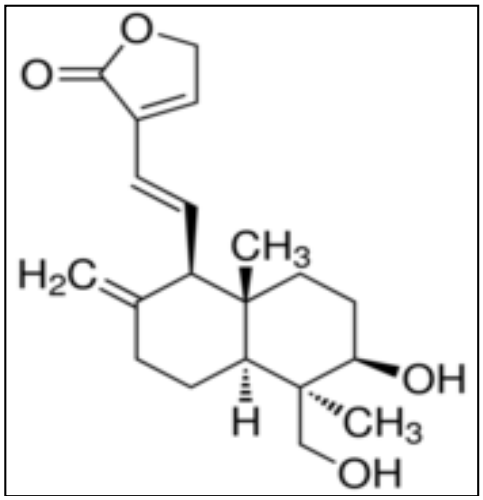

Fig 14: 14- deoxy-11, 12-didehydroandrographolide

Table: 6 Medicinal uses of *kalmegh*

Analgesic	**(pain killer) reduces swelling and cuts down exudation from capillaries; anti-inflammatory action probably mediated, in part, by adrenal function**
Antibacterial	fights bacterial activity; although *Andrographis* appears to have weak direct antibacterial action, it has remarkably beneficial effect in reducing diarrhea and symptoms arising from bacterial infections
Antiperiodic	counteracts periodic/intermittent diseases, such as malaria
Antipyretic	fever reducer - both in humans and animals, caused by multiple infections or by toxins
Antithrombotic	blood clot preventative
Antiviral	inhibits viral activity
Cancerolytic	Fights and kills cancer cells
Cardioprotective	protects heart muscles
Choleretic	alters the properties and flow of bile
Depurative	cleans and purifies the system, particularly the blood
Digestive	promotes digestion
Expectorant	promotes mucus discharge from the respiratory system
Hepatoprotective	protects the liver and gall bladder
Hypoglycemic	blood sugar reducer
Immune Enhancement	increases white cell phagocytosis, inhibits HIV-1 replication, and improves CD_4 and T-lymphocyte counts
Laxative	aids bowel elimination
Sedative	relaxing herb, though not with the same effect as the accepted herbal sedatives, valerian root, hops, skullcap, etc.
Thrombolytic	blood clot buster

4.2 Pharmacological activities

4.2.1 Immuno-modulatory activity

The ethanolic extract and purified diterpene and rographolides of *kalmegh* induced significant stimulation of antibody and delayed type hypersensitivity (DTH) response to sheep red blood cells (SRBC) in mice (Puri *et al*., 1993) [54]. In a study there were six known compounds isolated from *kalmegh viz*., andrographolide; 14-deoxy-11,12-didehydroandrographolide; and rograpanin; 14- deoxyandrographolide; (+/-)- 5- hydroxy-7,8-dimethoxyflavanone; and 5-hydroxy- 7,8-dimethoxyflavone and one Novel bis-andrographolide from the aerial parts of *kalmegh* and were found effective against HIV and cytotoxic activity (Reddy *et al*., 2005) [61]. The immunomodulatory properties of a diterpene lactone andrographolide and a standardized preparation (Coded name -Kan Jang) of *A. paniculata* were investigated. Proliferation of peripheral blood lymphocytes (PBL) induced by phyto hem agglutinin (PHA) was enhanced by co stimulation with Andrographolide and Kan Jang. At the same time Andrographolide and Kan Jang inhibit spontaneous proliferation of PBL in vitro (Panossian *et al*, 2002) [50]

4.2.2 Antioxidant activity

Trivedi *et al*, (2001) [80] in an experiment studied the effect of the *kalmegh* on antioxidant activity in mice by using the enzymes y- Glutamyl transpeptidase, glutathione- S-transferase, and lipid peroxidation compared to Benzene hexa Chloride (BHC). The activities of antioxidant enzymes like superoxide dismutase, catalase, glutathione peroxidase, and the levels of glutathione were decreased following the BHC effect.

Kamdem *et al.* in 2002 [26] in an experiment found the reaction mechanism of the superoxide scavenging activity of neoandrographolide isolated from *kalmegh*. It was hypothesized that neoandrographolide might scavenge free radicals by donating the allylic hydrogen of the unsaturated lactone ring. It was found that the stoichiometry of the reaction between neoandrographolide and superoxide radical generated from KO_2 in DMSO was 2: 1. One major reaction product was isolated and determined to be a diacid formed by the opening of the lactone ring. The antiradical activity of neoandrographolide proceeded by hydrogen abstraction from carbon C-15. Sheeja *et al*. 2007 in a study also concluded that

the methanolic extract of *kalmegh* was found effective to inhibit the formation of oxygen derived free radicals such as superoxide (32%) hydroxyl radicals (80%), lipid peroxidation (80%), and nitric oxide (42.8%) in in vitro system.

4.2.3 Antidiabetic activity

Antidiabetic property of *kalmegh* was confirmed by Borhanuddin *et al.* 1993 [7] and Husen *et al.* 2004 [24] in aqueous extract and by Zhang *et al.* 2000 in ethanolic extract of plant samples. Along with antihyperglycaemic property, the ethanolic extract may also reduce oxidative stress in diabetic rats. Further, it was concluded by Yu *et al*. in 2003 [91] that the andrographolide was responsible for the antihyperglycemic activity. Finally in 2006, the antidiabetic potential of *A. paniculata* was found to restore impaired estrous cycle in alloxan- induced diabetic rats. (Reyes *et al*., 2006) [63].

4.2.4 Hepatoprotective activity

Andrographolide has a significant dose-dependent protective activity against paracetamol-induced toxicity on ex vivo preparation of isolated rat hepatocytes (Visen *et al*., 1993) [86]. In the same year Kapil *et al*. 1993 [28] also proved the protective effects of *kalmegh* on hepatotoxicity induced in mice by carbon tetrachloride.

4.2.5 Prevention of common cold

A number of clinical studies have been done to prove that andrographolide isolated from *kalmegh* have protective effect against common cold. In a controlled study, andrographolide was also found to have beneficial effect on tiredness, shivering, sore throat, muscular ache, rhinitis, sinus pains and overall disease (Caceres *et al.,* 1999 [8]; Hancke *et al*., 1995 [17]; Melchior *et al.,* 1997) [41]. The inhibitory activity of andrographolide against common cold may be due to its immuno-stimulant effect. As a preventive for common cold, studies showed that andrographolide may increase body's resistance to infection by stimulating the production of antibodies and large white blood cells that scavenge foreign matter (Caceres *et al*., 1997, Puri *et al*., 1993) [54, 9].

4.2.6 Antipyretic activity

According to Indian, Thai and Chinese traditional medicine, *Andrographis paniculata* dispels heat and removes toxin, which makes it a good drug for treatment of infectious fever causing diseases. The ability of andrographolide to reduce fever has been demonstrated in several experiments. In rat studies, it has been shown that andrographolide can lower the fever produced by different fever inducing agents, such as bacterial endo-toxins, pneumococcus, hemolytic streptococcus, typhoid, paratyphoid and the chemical 2, 4-dinitrophenol (Deng, 1978) [12]. It was also found that andrographolide is as effective as the same dose of aspirin in reducing fever (Madav *et al.,* 1995 [37]; Vedavathy and Rao, 1991) [83].

4.2.7 Anti- allergic activity

Andrographis paniculata is used for the treatment of allergic manifestations as well as complications related to skin. Earlier studies have also supported its use in the treatment of dermatological diseases (Mukherjee, 1976) [44]. A study done by Gupta *et al.,* (1998) [15] revealed that andrographolide and neoandrographolide, active constituents of *Andrographis paniculata* shown anti-allergic activity. The molecules were tested for anti-passive cutaneous anaphylaxis (PCA) and mast cell stabilizing activities in rats. It was observed that both andrographolide and neoandrographolide significantly inhibited PCA in a dose dependant manner. They also significantly protected mast cell degranulation induced by compound 48/80 or egg albumin. The mechanism behind the anti-allergic activity of andrographolide seemed to be due to its mast cell stabilizing property.

4.2.8 Antidiarrhoeal activity

Extracts of *A. paniculata* have been shown to have antidiarrhoeal activity in *E. coli* infected diarrhoea (Gupta *et al*., 1990) [16]. Andrographolide showed similar activity to loperamide, the most common antidiarrhoeal drug. In other clinical studies, andrographolide has been shown to produce significant inhibition of bacterial diarrhoea and dysentery in patients (Deng. 1978) [12], which may be due to the antibacterial activity of the molecule.

4.2.9 Anti-HIV activity

Active metabolite and most important pharmacologically active andrographolide synthesized in *kalmegh* have great promise for the treatment of viral infections related to HIV. Andrographolide prevents transmission of the virus to other cells and stop the progress of the disease by modifying the cellular signal transduction process as andrographolide interferes with key enzymes (Cyclin dependent kinase CDK) responsible for transfer of phosphates, which helps in viral reproduction (Holt and Linda., 1998) [21].

Table: 7 Mechanisms of action of different pharmacological activities

SI. No.	Pharmacological activities	Mechanism of action	Source
1	Hepatoprotective activity	Prevention of oxidation, inhibition of cytochrome P-450, stimulation of hepatic regeneration and inhibition of microsomal enzymes or lipid peroxidation	Handa and Sharma.,1990 Kapil *et al.,* 1993 [28] Joshi and Magar., 1952 [25] Rana and Avadhoot., 1991 [58]
2	Antipyretic activity	Stimulation of immune system	Trivedi and Rawal., 2001 [80] Caceres *et al.,* 1997 [9]
3	Anti-inflammatory activity	Inhibits free radical production by modulation of protein kinase C (PKC)- dependent pathway and down-regulates up-expression of Mac-1, an essential integrin for neutrophil adhesion and transmigration	Vedavathy and Rao., 1991 [83] Nigam *et al.,* 1982 [48]
4	Antimicrobial activity	Antioxidant activity, particularly by reactivation of superoxide dismutase (SOD)	Shen *et al*., 2000 [73]
5	Antidiarrhoeal activity	Due to anti-bacterial activity	Madav *et al.,* 1995 [37]

6	Cardiovascular activity	Activates fibrinolysis, increases blood clotting time, inhibits PAF-induced platelet aggregation and prevent induction of clot. Hypotensive effect possibly by reducing circulating angiotensin converting enzymes (ACE) in the plasma and by reducing free radical generation	Chander *et al*., 1995 [10] Gupta *et al*., 1990 [16] Batkhuu *et al*., 2002 Bhatnagar., 1961 [6] Misra *et al*., 1992 [43] Singha *et al*., 2003 [75]
7	Anti-hyperglycemic activity	Increases glucose utilization to lower plasma. Glucose in diabetic rats lacking insulin and inhibits oxidative stress.	Wang and Zhao., 1993 [87] Zhao and Fang., 1990 [93]
8	Anti cancer and immunomodulatory activity	Activation of antigen specific response and nonspecific immune response, down modulation of humeral and cellular adaptive immune responses, interference with T cell proliferation and cytokine release in response to allogenic stimulation.	Sinha *et al*., 2000
9	Anti-HIV activity	Prevents transmission of virus to other cells, stops progress of disease by modifying cellular signal transduction, and inhibits C-mos-kinase, involved in HIV propagation.	Tripathi and Tripathi., 1991

5. Conclusion

We conclude from the vast literature study and experimental results analysis that *Andrographis paniculata* is an important medicinal, industrial cash crop which finds its immense utility for treatment of various diseases, ailments etc. Due to its pharmacological properties, the *kalmegh* herb is collected indiscriminately from the wild sources causing a sharp decline in the availability of this herb to the industry. Taking great concern of the useful benefits of the plant, there is a tremendous scope and need to take *kalmegh* as commercial crop for large scale cultivation by adopting efficient agronomic/crop management practices with an objective to enhance the yield, productivity and quality of produces without endangering the natural resource base.

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