

Green Chiryata (*Andrographis paniculata*): A potential blood purifier

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Abstract— *Andrographis paniculata* is a commonly used therapeutic herb in conventional systems of medicine like Siddha, Ayurveda, Unani, and Folk. It is also known as 'Kalmegh', "wonder herb", "King of Bitters" and "BhuiNeem". This plant possesses therapeutic properties like anti-hepatotoxic, anti-inflammatory, anti-diabetic, anti-pyretic, anti-bacterial, anti-viral, due to the presence of a variety of phytochemical constituents in it. Andrographolide is one of the main compound of Kalmegh which is associated with its therapeutic properties. It is being widely used for centuries in Asia, America and Africa continent for the treatment of diseases such as cancer, diabetes, high blood pressure, ulcer, leprosy, bronchitis, skin diseases, flatulence, colic, influenza, dysentery, dyspepsia and malaria. The present review is mainly based upon its ayurvedic view also describing the past and present research studies on *Andrographis paniculata* for its therapeutic uses and pharmacological activities to fill the gap in research for the development of herbal formulations.

Keywords— Kalmegh, Rasapanchak, Andrographolide, Anti-pyretic, Anti-viral, Anti-diabetic.

I. INTRODUCTION

Herbal medicinal plants are integral part of human life to fight the infections and sufferings from ancient times. Use of these medicinal plants for the treatment of human diseases is a core component at primary health care level due to their availability, acceptability, compatibility, and affordability. Traditional medicinal uses of these plants are well defined in Indian traditional Ayurvedic system. Kalmegh (*Andrographis paniculata*), is one of the major medicinal plant defined in Ayurveda, also called "King of Bitters", Maha-tita or Bhui-neem belongs to the *Acanthaceae* family. The genus *Andrographis* has 40 species out of which 19 species are found in India. The two species of Kalmegh i.e. *Andrographis paniculata* (Fig. 1) and *Andrographis alata* possess high therapeutic properties as compare to other species [1,2]. The taste of Kalmegh is as similar as of Neem (*Azadirachta indica*, A. Juss.). Diterpenoids, flavonoids and polyphenols are the major phytochemical constituents present in the plant as per reported scientific data [3,4]. Out of all bioactive constituents andrographolide is the major compound that is found in the plant in terms of bioactive properties and abundance. The plant has been utilized in India to treat gastrointestinal tract infections, upper respiratory infections, fever, herpes, sore throat, and a variety of other infectious diseases [5,6,7]. Indian pharmacology states that this plant is predominant constituents of at least 26 ayurvedic formulations [8]. It also possesses "Blood purifying" activity that is used in the treatment of leprosy, gonorrhoea, scabies, skin problems [9]. Various medicine of *A. paniculata* are available in the market as anti-malarial [10], anti-inflammatory, anti-oxidant [11], antihistatic [12], antihyperglycemic [13], anthelmintic [14], antibacterial [15], antipyretic [16] and anticancer supplements. Taxonomical classification [17,18,19] and vernacular names [20] are shown in the table 1 and 2 respectively.



Figure 1. Kalmegh (*Andrographis paniculata*)

Table 1. Taxonomical Classification of Kalmegh (*Andrographis paniculata*)

Taxonomic rank	Taxon
Kingdom	Plantae
Division	Angiosperm
Order	Lemiales
Class	Magnoliopsida
Family	Acanthaceae
Genus	<i>Andrographis</i>
Species	<i>A.paniculata</i>
Common Name	Kalmegh, Kirayat

Table 2. Vernacular names of *Andrographis paniculata*

Sanskrit	Kālamegha , Bhūnimba
Hindi	Kirayat
English	Green chirayta
Assamese	Chiorta
Bengali	Kālmegh
Oriya	Bhūnimba
Gujrati	Kariyatu
Tamil	Nilavembu, Sirunangai, Siriyanga
Kannada	Nelaberu
Telugu	Nelavemaa
Marathi	Oli-kiryata
Persian	Naine- havandi
Chinese	Chuan Xin Lian Arab
Arab	Quasabhava
Malayalam	Kiriyattu

Botanical Description of *Andrographis paniculata*

Kalmegh is a yearly, branched, herbal plant that grows up to the height of 30-110 cm in moist and dark places. The stem is quadrangular, slender, branched, easily broken, and dark green, square in cross-section with longitudinal furrows [21]. The shape of the leaves is lanceolate, glabrous, 2-12 cm in length and 1-3cm wide with hairless blades long up to 8cm long and 2.5cm wide. Flowers are small, borne in branched racemes with the various botanical features of calyx, linear, corolla tube narrow, about 6mm long and the tube is shorter than the limb, bilabiate (two limbed). The upper limb is obligate, white with yellow tip and the lower limb is widely cuneate, 3 lobed, white with violet marking. The fruit is 1-2 cm long and 2-5mm wide capsulated, erect, linear-oblong, compressed, acute at both ends, thin, hairy with yellow-brown seeds inside. The seeds are small and sub quadrate [22,23].

Geographical Distribution of *Andrographis paniculata*

Andrographis paniculata grows abundantly in southwards region around the world i.e. India, Sri Lanka, Pakistan, Thailand, Malaysia, and Indonesia. But India is the major producer of this plant [24]. It is cultivated in the rainy season. In India, it is distributed in various states like Madhya Pradesh, Chhattisgarh, Orissa, Maharashtra, Assam, West Bengal, Uttar Pradesh, Tamil Nadu, Karnataka, and Kerala [25].

Phytochemical Constituents of *Andrographis paniculata*

A. paniculata has many chemical constituents which is present in its roots and aerial parts. The constituents may vary due to diverse factors such as geographical region, harvest time and processing method [26,27]. There are various metabolites found in the plant. These metabolites are terpenoids, flavonoids (flavones), noriridoides, xanthenes, polyphenols and marco elements.

1. **Terpenoids:** Diterpenoid lactones are the most common metabolite extracted from *A. paniculata*. Andrographolide has a crystalline, colorless and very bitter in taste [28] and was first

isolated in pure form by Gorter in 1911. The chemical mostly extracted from the aerial parts including deoxyandrographolide and neoandrographolide. Other than diterpenes, 23 unusual carbon terpenoids are isolated from the roots and aerial parts of the plant [29]. Some terpenes of *A. paniculata* shows in the table 3.

2. **Flavonoids:** Flavones are the major flavonoids present in the whole plant of *A. paniculata*. 5, 7, 2', 3'-tetramethoxyflavone, 5-hydroxy-7, 2', 3'-trimethoxy flavones, 5-hydroxy-7, 2', 6'-trimethoxyflavone, 7-O-methyl-dihydro-wogonin, 7-O-methyl-wogonin, Flavone-1, 2'-methylether, 7-O-methyl-wogonin-5-glucoside, Flavone-1, 2'-O-glucoside, 5-hydroxy-7, 8, 2', 5'-tetramethoxyflavone, Dihydro-skullcapflavone, 5-hydroxy-7, 8, 2, 3'-tetramethoxyflavone are the flavonoids isolated from this plant [29,30,32,47,48,50,51,52].

3. **Miscellaneous Compounds:** Many other compounds have been isolated from roots of *A. paniculata*. The isolation is done by thin layer chromatography (TLC) and column chromatography. Four xanthenes were extracted by TLC and characterized by infrared radiation, mass and nuclear magnetic resonance spectroscopy. The isolated compounds are 1, 8-dihydroxy-3,7-dimethoxy-xanthone, 4,8-dihydroxy-2,7-dimethoxy-xanthone, 1,2-dihydroxy-6,8-dimethoxy-xanthone and 3,7,8-trimethoxy-1-hydroxy-xanthone. From the roots of plant five rare noriridoids designated andrographolide A-E, along with curvifloruside [30]. Trace elements (Cr, Mn, Co, Ni, Zn, Cu, Se, Rb, Sr and Pb) and macro-element (K and Ca) are also identified in the roots [31]. Cinnamic acid, caffeic acid, ferulic acid and chlorogenic acid were also isolated from the whole plant [32,33]. Arabinogalactan, 1, 8-dihydroxy-3,7-dimethoxy-xanthone, 4,8-dihydroxy-2,7-dimethoxy-xanthone, 1,2-dihydroxy-6,8-dimethoxy-xanthone, 3,7,8-trimethoxy-1-hydroxy-xanthone, Andrographidoid A, Andrographidoid B, Andrographidoid C, Andrographidoid D, Andrographidoid E are some miscellaneous compounds of *A. paniculata* [52,53]. Chemical structure of some of the major phytochemicals are shown in figure 2.

Table 3. Terpenes of *A. paniculata*

Andrographolide	Leaves/aerial [29,35,36,37,38]
Neoandrographolide	Leaves/aerial [32,39,41]
14-deoxyandrographolide	Aerial parts [36,42]
Andrographoside	Leaves/aerial parts [33]
14-deoxy-11, 12-didehydroandrographolide	Aerial parts [40,43]
19-O-β-D-glucopyranosyl-ent-labda-8(17), 13-dien-15, 16, 19-triol	Aerial parts [44]
8α-methoxy-14-deoxy-17β-hydroxyandrographolide	Aerial parts [45]
Andrographolactone	Aerial parts [44]
3, 13, 14, 19-tetrahydroxy- ent-labda-8(17), 11-dien-16, 15-olide and 3, 19 isopropylidene- 14-deoxy- ent-labda-8(17), 13-diene-16, 15-olide	Aerial parts [46]
10, 14-deoxy-15-isopropylidene-11,12-didehydroandrographolide	Aerial parts/roots [46]
3,7,19-trihydroxyl-8,11, 13- ent-labdatriene-15, 16-olide and 8α,17β-epoxy-3, 19-dihydroxy-11,13-ent-labdatrien-15, 16-olide D	Aerial parts [46]
Andrograpanin	Leaves [46]

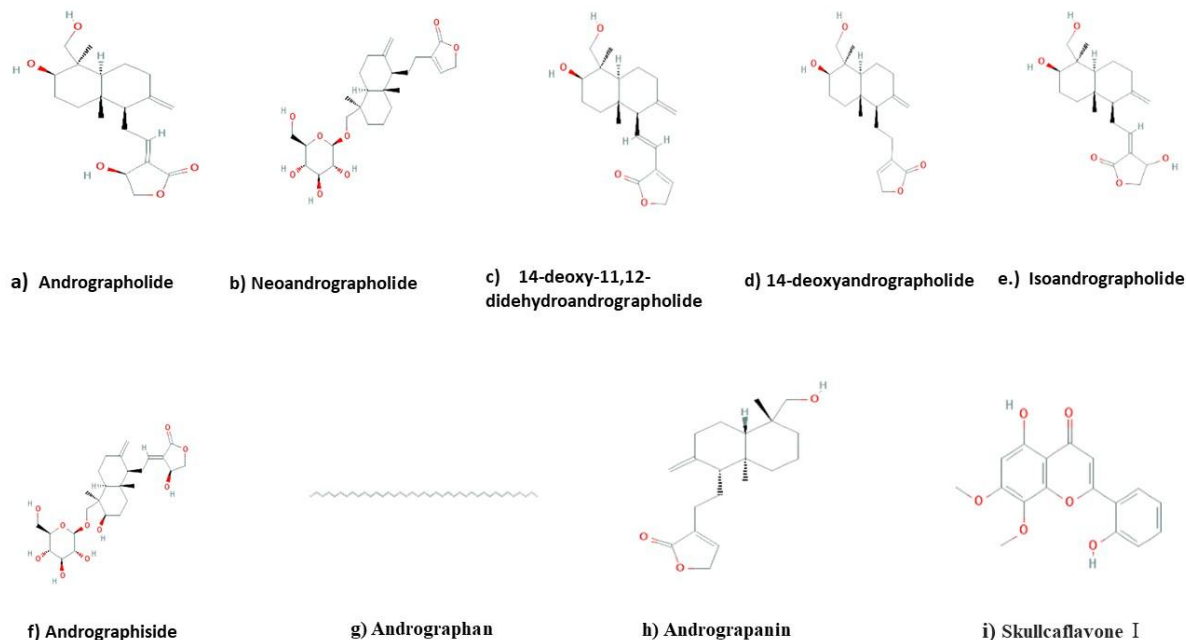


Figure 2. Structures of Some Major Chemical Constituents of *A. paniculata*

Folk view on Kalmegh/Green Chiryta

Plants have been used as a source of medicine across the globe in almost every culture, since ancient times. As per the reports of WHO, almost 80% population of the world depends upon the conventional system of medicine for maintaining their health [54,55]. Rural communities and tribal populations depend upon plants to fulfil their basic health needs. They have knowledge regarding the traditional use of plants which have verbally been passed from one generation to another generation. Kalmegh is one of the significant herb used in the conventional medicine system. Asian and European countries are using leaves and roots of the Kalmegh plant since ancient times for treating a wide range of health issues. For instance, Tribal people of Sonebhadra District of Uttar Pradesh and memba tribe of Arunachal Pradesh use roots and leaves of this plant against varieties of diseases like cholera, colic disease, diarrhea, dysentery, fever, filaria, malaria, stomach complaints, tonic. Tribal people of Sonebhadra uses the leaves extract with milk against snake bites. Memba tribe also utilizes Kalmegh as an antihelmintic agent [56,57,58]. Rural community of Tryambakeshwar hill of Nashik district, Maharashtra, uses Kalmegh plant powder in treating warts. They use Kalmegh leaf in insect bites and the whole plant is used in hepatitis and inflammation [59]. As it has blood purifying property, therefore it is used for leprosy, gonorrhea, scabies, boils, skin eruptions, and chronic and seasonal fever in many conventional systems [60,61]. Kalmegh juice or infusion treats irregular bowel conditions, enhances appetite, and relieve griping in infants [62,63]. In the conventional medicine system of Malaysia, Kalmegh is used in diabetes and hypertension [64]. In the Scandinavian and Japanese and Thai traditional medicine system, it is used against common cold and fever [65].

Ayurvedic View

Ayurveda is the conventional medical science that gives us abundant knowledge of Dravyas or drugs which we get from natural resources. The therapeutic plant is the major source of Ayurvedic medicines and the primary component as per their availability, compatibility, and affordability [66]. The literature of Ayurveda has been described for many herbal plants to treat various ailments. One such herb is “Kalmegh”.

Kalmegh means "Dark cloud" because the appearance of the plant is like a black cloud in the blue sky. The Sanskrit name of the plant is “Bhunimba” also known as Bhui-neem, meaning "neem of the ground". The name is recommended as per strong bitter taste just like the neem [67]. In ayurveda, the therapeutic use of drug (Darvya) is mainly based on its properties (Rasa panchak) [68]. The rasa panchak of kalmegh is shown in the table 4.

Table 4. Rasa Panchak (Properties) of Kalmegh as per Ayurveda [68]

Sanskrit/English	Sanskrit/English
Virya/Potency	Ushana/Hot
Vipak/Metabolic Property	Katu/Pungent
Guna/Physical Property	Tikat/Bitter
Rasa/Taste	Laghu,Ruksha/Little,Dry

Action (Karma) of Kalmegha: Reduce Kapha (Water and earth component) and Pitta (Fire and water component) Dosh (disorder) [69].

Properties of Green Chiryta/Kalmegh [70]

1. Abhiyantar Pachansansthan: It works on the GIT, Dipana (appetizer), Pachana (digestive), Jwaraghna (antipyretic), Krimighna (wormicidal) and also kills the parasites.
2. Raktavah Sansthan: It increases the blood circulation and Raktashodhak (Blood purifier).

3. Sansthanik Karma Baham: Used as an Vedna sansthapak analgesic or pain killers.
4. Taapkaram: Used for the treatment of malaria and severe fever.
5. Tavcha: Used for the skin infections.
6. Satambhikaran: Used for the treatment of chronic fever

Modern View on Green Chiryta/Kalmegh

Adulteration is the major issue in today's scenario which is faced by the Global herbal market. It is the main disadvantage in the promotion of herbal drugs and that's why people have lost faith in these medicines [71,72,73,74,75,76]. One of the most used practices is species adulteration. In the herbal drug market species, adulteration has been suspected for quite a while [77]. It has adverse impacts on consumer health [78]. One of the most popular incidents of species adulteration is from China when kidney failure of more than 100 women occurred due to adulteration of species i.e. roots of *Stephania tetrandra* which is an anti-inflammatory agent with the roots of a toxic plant called *Aristolochia fang chi* [79]. Many other practices are incorporated in the trade market of herbal drugs in modern times which are directly or indirectly degrading the quality of herbal medicines. One of them is the use of artificially manufactured material that looks like the original drug. This is the most common practice of adulteration in the case of expensive herbal drugs [80,81,82]. Due to the presence of several adulterants the rate of toxicity has increased and also the high cost is the associated factor of adulteration [83].

Reported Therapeutic and Pharmacological Properties of *Andrographis paniculata*

Anti-bacterial: Antibacterial activity of *Andrographis paniculata* was tested in an experimental study against four bacterial namely *Staphylococcus sp.*, *Escherichia coli*, *Salmonella sp.* and *Pseudomonas sp.* From this study it was found that the methanol leaf extract has significant antibacterial activity. It showed maximum inhibitory action against *E. coli* than the rest three bacterial species [84]. Findings of one more study revealed that the chloroform, aqueous, methanol, petroleum ether extracts of Kalmegh have anti-bacterial properties. These extracts were tested in *E. coli* and *S. aureus* bacterial species.

Hepatoprotective: Hepatoprotective action was evaluated in a study conducted on paracetamol-induced liver injury in a mice model. Different plant formulations were used in the study. The formulation which contain *A. paniculata* showed significant hepatoprotective potential [85].

Anti-pyretic: As per the study conducted on pyrogenic polysaccharide – induced hyperpyrexia in male albino rats, the alcoholic extracts of *A. paniculata* and the other two species of *Andrographis* have inhibiting properties against hyperpyrexia [86].

Anti-cancer: Methanolic extract of *A. paniculata* has anti-cancer property and it is shown in the study which was conducted to check the anticancer activity in human cancer cells. The result showed that methanolic fraction dichloromethane inhibits the proliferation of colon cancer cells and Andrographolide fraction obtained through further

fractionation of dichloromethane exhibited anticancer activity on various cancer cells [87].

Anti-diabetic: A study was conducted on high fructose-fat-fed rats which showed that the purified extract and andrographolide significantly lowered- down the blood glucose level and triglyceride, and LDL at a particular dose [88]. Another study conducted on streptozotocin-induced diabetic rats showed that chloroform fractions of ethanol extracted from the leaves of Kalmegh had anti-diabetic impacts (100 mg/Kg body weight 29.48%) on lowering down the glucose level of the blood. Four compounds were further isolated from the chloroform extract i.e. sitosterol, andrographolide, lupeol, and quercetin showed good anti-diabetic activity [89].

Anti-fertility: The anti-fertility potential of *A. paniculata* was evaluated during a study on 3-month-old male Wistar albino rats. The findings showed that andrographolide administration for 48 days at two dose levels, had a significant effect on sperm count and motility and caused abnormalities of the cauda epididymal spermatozoa. Thus due to the presence of andrographolide, Kalmegh is used as an anti-fertility agent [90].

Anti-oxidant: As per the research report, the anti-oxidant property is strongly attributed to the methanolic extract of *A. paniculata* [91]. Another investigative study in lymphoma bearing AKR mice showed that aqueous extract has antioxidant potential [92].

Analgesic: The *in-vitro* study on carrageenan-induced paw edema models i.e. Swiss albino mice and Wistar albino rats showed that ethanolic extract of leaves of Kalmegh has analgesic and anti-inflammatory properties [93].

Anti-HIV: The *in-vitro* study on de-hydro andrographolide succinic acid monoester (DASM) and andrographolide showed inhibitory action against the Human immunodeficiency virus [94].

Anti-venom: The *in vivo* and *in vitro* examinations have shown that Andrographolide has anti-venom activity [95]. The cytotoxic levels also determined by the use of cell lines.

Anti-diarrheal: A study conducted on an animal model revealed that the alcoholic extract of *A. paniculata* has anti-diarrheal action against *E. coli* [96].

Antiplatelet: *A. paniculata* in an *in-vivo* study showed inhibitory action against platelet aggregation [97].

II. CONCLUSION

After doing ayurvedic and modern science based literature study, it is concluded that *A. paniculata* (Kalmegh) is a therapeutically important herb for disorders like infections, fever, respiratory disorders, snake bites, worm's infections and many more. Its active phytochemical compounds are associated with significant therapeutic properties. As per the reported study, Kalmegh show various other pharmacological activities like anti-inflammatory, anti-diabetic, anti-cancerous, anti-venom, antipyretic, hepatoprotective and many more. After reviewing all the ayurvedic and modern scientific aspects of Kalmegh, this medicinal herb can be advocated as a safe and of great healthcare importance for general mankind. Furthermore, because of the presence of several bioactive compounds and low toxicity profile, this plant can be explored

for the development of herbal formulations for the treatment of many diseases.

REFERENCES

- [1] Madav S, Tripathi HC, Mishra SK. Analgesic, antipyretic and antiulcerogenic effects of andrographolide. *Indian Journal of Pharmaceutical Sciences*. 1995;57(3):121.
- [2] Sheeja K, Guruvayoorappan C, Kuttan G. Antiangiogenic activity of *Andrographis paniculata* extract and andrographolide. *International immunopharmacology*. 2007 Feb 1;7(2):211-21.
- [3] Rao YK, Vimalamma G, Rao CV, Tzeng Y: Flavonoids and andrographolides from *Andrographis paniculata*. *Phytochemistry*. 2004, 65: 2317-2321. 10.1016/j.phytochem.2004.05.008.
- [4] Xu C, Chou GX, Wang ZT: A new diterpene from the leaves of *Andrographis paniculata* Nees. *Fitoterapia*. 2011.
- [5] Mishra SK, Sangwan NS, Sangwan RS. Phcog rev.: Plant review *Andrographis paniculata* (Kalmegh): A review. *Pharmacognosy Reviews*. 2007 Jul;1(2):283-98.
- [6] Nadkarni A. *Nadkarni's Indian Materia Medica*. Nadkarni's Indian Materia Medica. 1954.
- [7] Gupta S, Choudhry MA, Yadava JN, Srivastava V, Tandon JS. Antidiarrhoeal activity of diterpenes of *Andrographis paniculata* (Kalmegh) against *Escherichia coli* enterotoxin in in vivo models. *International Journal of Crude Drug Research*. 1990 Jan 1;28(4):273-83.
- [8] Kumar RA, Sridevi K, Kumar NV, Nanduri S, Rajagopal S. Anticancer and immunostimulatory compounds from *Andrographis paniculata*. *Journal of ethnopharmacology*. 2004 Jun 1;92(2-3):291-5.
- [9] Kumar A, Dora J, Singh A, Tripathi R. A review on king of bitter (Kalmegh). *Int J Res Pharm Chem*. 2012;2(1):116-24.
- [10] Mishra K, Dash AP, Swain BK, Dey N. Anti-malarial activities of *Andrographis paniculata* and *Hedyotis corymbosa* extracts and their combination with curcumin. *Malaria journal*. 2009 Dec;8(1):1-9.
- [11] Sheeja K, Shihab PK, Kuttan G. Antioxidant and anti-inflammatory activities of the plant *Andrographis paniculata* Nees. *Immunopharmacology and immunotoxicology*. 2006 Jan 1;28(1):129-40.
- [12] Singh RP, Banerjee S, Rao AR. Modulatory influence of *Andrographis paniculata* on mouse hepatic and extrahepatic carcinogen metabolizing enzymes and antioxidant status. *Phytotherapy Research*. 2001 Aug;15(5):382-90.
- [13] Zhang XF, Tan BK. Antihyperglycaemic and anti-oxidant properties of *andrographis paniculata* in normal and diabetic rats. *Clinical and Experimental Pharmacology and Physiology*. 2000 May;27(5-6):358-63.
- [14] Siddhartha S, Archana M, Jinu J, Pradeep M. Anthelmintic potential of *Andrographis paniculata*, *Cajanus cajan* and *Silybum marianum*. *Pharmacogn J*. 2009 Dec 1;1:243.
- [15] Aniel Kumar O, Mutyala Naidu L, Raja Rao KG. In vitro antibacterial activity in the extracts of *Andrographis paniculata* Burm. F. *International Journal of PharmTech Research*. 2010 Apr;2(2):1383-5.
- [16] Chandra R, Kumarappan CT, Kumar J, Mandal SC. Antipyretic activity of JURU-01-a polyherbal formulation. *Global J. Pharmacol*. 2010;4(1):45-7.
- [17] Valdiani A, Kadir MA, Tan SG, Talei D, Abdullah MP, Nikzad S. Naine Havandi *Andrographis paniculata* present yesterday, absent today: a plenary review on underutilized herb of Iran's pharmaceutical plants. *Molecular biology reports*. 2012 May 1;39(5):5409-24.
- [18] Parixit B, Bharath C, Rajarajeshwari N, Ganapaty S. The genus *Andrographis*—a review, *International Journal of Pharmaceutical Sciences*. 2012; 4(1):1835-1856
- [19] Niranjan Reddy VL, Malla Reddy S, Ravikanth V, Krishnaiah P, Venkateshwar Goud T, Rao TP, Siva Ram T, Gonnade RG, Bhadbhade M, Venkateswarlu Y. A new bis-andrographolide ether from *Andrographis paniculata* nees and evaluation of anti-HIV activity. *Natural Product Research*. 2005 Apr 1;19(3):223-30.
- [20] Jarukamjorn K, Nemoto N. Pharmacological aspects of *Andrographis paniculata* on health and its major diterpenoid constituent andrographolide. *Journal of health science*. 2008;54(4):370-81.
- [21] Chadha YR. *The Wealth of India: Raw materials*, Vol. 1 A. Council of Scientific and Industrial Research, New Delhi, India. 1985;264.
- [22] Pholphana N, Rangkadilok N, Thongnest S, Ruchirawat S, Ruchirawat M, Satayavivad J. Determination and variation of three active diterpenoids in *Andrographis paniculata* (Burm. f.) Nees. *Phytochemical Analysis: An International Journal of Plant Chemical and Biochemical Techniques*. 2004 Nov;15(6):365-71.
- [23] Prajapati ND, Purohit SS, Sharma AK, Kumar T. A handbook of medicinal plants: A complete source book. In *A handbook of medicinal plants: a complete source book 2003* (pp. 554-554).
- [24] Niranjan A, Tewari SK, Lehri A. Biological activities of kalmegh (*Andrographis paniculata* Nees).
- [25] Katakya A, Handique PJ. A brief overview on *Andrographis paniculata* (Burm. f.) Nees., a high valued medicinal plant: Boon over synthetic drugs. *Asian J Sci Technol*. 2010 Oct;6:113-8.
- [26] Pholphana N, Rangkadilok N, Thongnest S, Ruchirawat S, Ruchirawat M, Satayavivad J. Determination and variation of three active diterpenoids in *Andrographis paniculata* (Burm. f.) Nees. *Phytochemical Analysis: An International Journal of Plant Chemical and Biochemical Techniques*. 2004 Nov;15(6):365-71.
- [27] Li W, Fitzloff JF. HPLC-PDA determination of bioactive diterpenoids from plant materials and commercial products of *Andrographis paniculata*. *Journal of liquid chromatography & related technologies*. 2004 Jan 1;27(15):2407-20.
- [28] Siripong P, Kongkathip B, Preechanukool K, Picha P, Tunsuwan K, Taylor WC. Cytotoxic diterpenoid constituents from *Andrographis paniculata* Nees leaves. *J Sci Soc Thailand*. 1992 Dec 1;18(4):187-94.
- [29] Reddy MK, Reddy MV, Gunasekar D, Murthy MM, Caux C, Bodo B. A flavone and an unusual 23-carbon terpenoid from *Andrographis paniculata*. *Phytochemistry*. 2003 Apr 1;62(8):1271-5.
- [30] Xu C, Chou GX, Wang CH, Wang ZT. Rare noriridoids from the roots of *Andrographis paniculata*. *Phytochemistry*. 2012 May 1;77:275-9.
- [31] Behera PR, Nayak P, Barik DP, Rautray TR, Thirunavoukkarasu M, Chand PK. ED-XRF spectrometric analysis of comparative elemental composition of in vivo and in vitro roots of *Andrographis paniculata* (Burm. f.) Wall. ex Nees—a multi-medicinal herb. *Applied Radiation and Isotopes*. 2010 Dec 1;68(12):2229-36.
- [32] Rao YK, Vimalamma G, Rao CV, Tzeng YM. Flavonoids and andrographolides from *Andrographis paniculata*. *Phytochemistry*. 2004 Aug 1;65(16):2317-21.
- [33] Kuroyanagi M, Sato M, Ueno A, Nishi K. Flavonoids from *Andrographis paniculata*. *Chemical and pharmaceutical bulletin*. 1987 Nov 25;35(11):4429-35.
- [34] Liu J, Wang ZT, Ge BX. Andrograpanin, isolated from *Andrographis paniculata*, exhibits anti-inflammatory property in lipopolysaccharide-induced macrophage cells through down-regulating the p38 MAPKs signaling pathways. *International immunopharmacology*. 2008 Jul 1;8(7):951-8.
- [35] Puri A, Saxena R, Saxena RP, Saxena KC, Srivastava V, Tandon JS. Immunostimulant agents from *Andrographis paniculata*. *Journal of Natural products*. 1993 Jul;56(7):995-9.
- [36] Matsuda T, Kuroyanagi M, Sugiyama S, Umehara K, Ueno A, Nishi K. Cell differentiation-inducing diterpenes from *Andrographis paniculata* Nees. *Chemical and Pharmaceutical Bulletin*. 1994 Jun 15;42(6):1216-25.
- [37] Cheung HY, Cheung CS, Kong CK. Determination of bioactive diterpenoids from *Andrographis paniculata* by micellar electrokinetic chromatography. *Journal of Chromatography A*. 2001 Sep 28;930(1-2):171-6.
- [38] Kleipool RJ. Constituents of *Andrographis paniculata* Nees. *Nature*. 1952 Jan;169(4288):33-4.
- [39] Chan WR, Taylor DR, Willis CR, Bodden RL, Fehlhaber HW. The structure and stereochemistry of neoandrographolide, a diterpene glucoside from *Andrographis paniculata* Nees. *Tetrahedron*. 1971 Jan 1;27(21):5081-91.
- [40] Jain DC, Gupta MM, Saxena S, Kumar S. LC analysis of hepatoprotective diterpenoids from *Andrographis paniculata*. *Journal of pharmaceutical and biomedical analysis*. 2000;22(4):705-9.
- [41] Yang M, Wang J, Kong L. Quantitative analysis of four major diterpenoids in *Andrographis paniculata* by ¹H NMR and its application for quality control of commercial preparations. *Journal of pharmaceutical and biomedical analysis*. 2012 Nov 1;70:87-93.
- [42] Wu D, Cao X, Wu S. Overlapping elution-extrusion counter-current chromatography: A novel method for efficient purification of natural cytotoxic andrographolides from *Andrographis paniculata*. *Journal of Chromatography A*. 2012 Feb 3;1223:53-63.

- [43] Aromdee C. Modifications of andrographolide to increase some biological activities: a patent review (2006–2011). Expert opinion on therapeutic patents. 2012 Feb 1;22(2):169-80.
- [44] Zou QY, Li N, Dan C, Deng WL, Peng SL, Ding LS. A new ent-labdane diterpenoid from *Andrographis paniculata*. Chinese Chemical Letters. 2010 Sep 1;21(9):1091-3.
- [45] Ma XC, Gou ZP, Wang CY, Yao JH, Xin XL, Lin Y, Liu KX. A new ent-labdane diterpenoid lactone from *Andrographis paniculata*. Chinese Chemical Letters. 2010 May 1;21(5):587-9.
- [46] Xu C, Chou GX, Wang ZT. A new diterpene from the leaves of *Andrographis paniculata* Nees. Fitoterapia. 2010 Sep 1;81(6):610-3.
- [47] Gupta KK, Taneja SC, Dhar KL, Atal CK. Flavonoids of *Andrographis paniculata*. Phytochemistry. 1983 Jan 1;22(1):314-5.
- [48] Varma A, Padh H, Shrivastava N. Andrographolide: a new plant-derived antineoplastic entity on horizon. Evidence-Based Complementary and Alternative Medicine. 2011 Jan 1;2011.
- [49] Zhou B, Zhang D, Wu X. Biological activities and corresponding SARs of andrographolide and its derivatives. Mini reviews in medicinal chemistry. 2013 Feb 1;13(2):298-309.
- [50] Lim JC, Chan TK, Ng DS, Sagineedu SR, Stanslas J, Wong WF. Andrographolide and its analogues: versatile bioactive molecules for combating inflammation and cancer. Clinical and Experimental Pharmacology and Physiology. 2012 Mar;39(3):300-10.
- [51] Kishore PH, Reddy MV, Reddy MK, Gunasekar D, Caux C, Bodo B. Flavonoids from *Andrographis lineata*. Phytochemistry. 2003 Jun 1;63(4):457-61.
- [52] Chao WW, Lin BF. Isolation and identification of bioactive compounds in *Andrographis paniculata* (Chuanxinlian). Chinese medicine. 2010 Dec;5(1):1-5.
- [53] Dua VK, Ojha VP, Roy R, Joshi BC, Valecha N, Devi CU, Bhatnagar MC, Sharma VP, Subbarao SK. Anti-malarial activity of some xanthenes isolated from the roots of *Andrographis paniculata*. Journal of Ethnopharmacology. 2004 Dec 1;95(2-3):247-51.
- [54] Dubey NK, Kumar R, Tripathi P. Global promotion of herbal medicine: India's opportunity. Current science. 2004.
- [55] Singh A, Dubey NK. An ethnobotanical study of medicinal plants in Sonbhadra District of Uttar Pradesh, India with reference to their infection by foliar fungi. Journal of Medicinal Plants Research. 2012.
- [56] Singh A, Singh GS, Singh PK. Medico-ethnobotanical inventory of Renukoot forest division of district Sonbhadra, Uttar Pradesh, India. 2012.
- [57] Rethy P, Singh B, Kagyung R, Gajurel PR. Ethnobotanical studies of Dehang–Debang Biosphere Reserve of Arunachal Pradesh with special reference to Memba tribe. 2010.
- [58] Kakulte VR, Gaikwad KN, Jadhav SV. Diversity of Ethnobotanical Plants Used by Rular Community of Tryambakeshwar Hill of Nashik District, Maharashtra, India. International Journal of Life sciences and Pharma Research. 2014.
- [59] Akbar S. *Andrographis paniculata*: a review of pharmacological activities and clinical effects. Alternative Medicine Review. 2011.
- [60] Deng WL. Outline of current clinical and pharmacological research on *Andrographis paniculata* in China. Newsl Chin Herb Med. 1978.
- [61] Dymock W, Warden CJ, Hooper D. Pharmacographia Indica 1, 69, republished by the Institute of Health and Tibbi Research under the auspices of Hamdard National Foundation. 1972.
- [62] Chopra RN, Chopra IC, Handa KL, Kapoor LD. Indigenous drugs of India Academic publishers. Calcutta-New Delhi. 1982.
- [63] Borhanuddin M, Shamsuzzoha M, Hussain AH. Hypoglycaemic effects of *Andrographis paniculata* Nees on non-diabetic rabbits. Bangladesh Medical Research Council Bulletin. 1994.
- [64] Jarukamjorn K, Nemoto N. Pharmacological aspects of *Andrographis paniculata* on health and its major diterpenoid constituent andrographolide. Journal of health science. 2008.
- [65] Chaudhari A, Singh B. IJAMS International Journal of Ayurveda & Medical Sciences.
- [66] Mudgal D. Dravyagun Vigyan. Ayurvedic Sanskrit Hindi Pustak Bhandar. 2019.
- [67] Sharma PV. Dravyagun Vigyan. Chaukambha Bharti Academy, Varanasi, Reprint. 2019
- [68] Pandey G. Dravyaguna Vijnana. Chowkhamba Krishnadas Academy, Varanasi, Reprint 2004
- [69] Sehgal H, Singh B, Thapliyal S. Role of Kalmegha (*Andrographis paniculata* (burm. f.) wall. Ex nees) in treating vatarakta (gout). Journal of Drug Delivery and Therapeutics. 2018 Nov 15;8(6):98-101.
- [70] Tewari NN. Some crude drugs: source, substitute and adulterant with special reference to KTM crude drug market. Sachitra Ayurved. 1991.
- [71] Shukla P, Pawar RM. OA01. 22. Quality aspect and variability observed in physico-chemical characteristics and mineral content of ayurvedic herbo mineral formulations from Indian market. Ancient Science of Life. 2012.
- [72] Sunita G. Substitute and adulterant plants. Substitute and adulterant plants.1992.
- [73] Uniyal MR, Joshi GC. Historical view of the basic principles of the identification of controversial drugs, problems and suggestions. Sachitra Ayurved. 1993.
- [74] Saraswathy A. Adulterants and substitutes in Ayurveda. Sachitra Ayurved. 2001.
- [75] Gupta AK. Quality standards of Indian medicinal plants. Volume 1. Quality standards of Indian medicinal plants. Volume 1.2003.
- [76] Song J, Yao H, Li Y, Li X, Lin Y, Liu C, Han J, Xie C, Chen S. Authentication of the family Polygonaceae in Chinese pharmacopoeia by DNA barcoding technique. Journal of Ethnopharmacology. 2009.
- [77] Newmaster SG, Grguric M, Shanmughanandhan D, Ramalingam S, Ragupathy S. DNA barcoding detects contamination and substitution in North American herbal products. BMC medicine. 2013.
- [78] Gilbert N. Herbal medicine rule book: can Western guidelines govern Eastern herbal traditions? Nature. 2011.
- [79] Mitra SK, Kannan R. A note on unintentional adulterations in Ayurvedic herbs. Ethnobotanical Leaflets. 2007.
- [80] Poornima B. Adulteration and substitution in herbal drugs a critical analysis. IJRAP. 2010.
- [81] Roy A, Mallick A, Kaur A. Adulteration and substitution in Indian medicinal plants. IJPRBS. 2013.
- [82] Goswami A, Barooah PK, Sandhu JS. Prospect of herbal drugs in the age of Globalization-Indian scenario. J Scientific Industrial Research. 2002.
- [83] Shalini VB, Narayanan JS. Antibacterial activity of *Andrographis paniculata* Nees against selective human pathogens. African Journal of Microbiology Research. 2015.
- [84] Das P, Srivastav AK. Phytochemical extraction and characterization of the leaves of *Andrographispaniculata* for its anti-bacterial, anti-oxidant, anti-pyretic and anti-diabetic activity. Int. J. innov. res. sci. eng. technol. 2014.
- [85] Girish C, Koner BC, Jayanthi S, Rao KR, Rajesh B, Pradhan SC. Hepatoprotective activity of six polyherbal formulations in paracetamol induced liver toxicity in mice. Indian Journal of Medical Research. 2009.
- [86] Balu S, Boopathi CA, Elango V. Antipyretic activities of some species of *Andrographis* Wall. Ancient science of Life. 1993.
- [87] Kumar RA, Sridevi K, Kumar NV, Nanduri S, Rajagopal S. Anticancer and immunostimulatory compounds from *Andrographis paniculata*. Journal of ethnopharmacology. 2004.
- [88] Nugroho AE, Andrie M, Warditiani NK, Siswanto E, Pramono S, Lukitaningsih E. Antidiabetic and antihyperlipidemic effect of *Andrographis paniculata* (Burm. f.) Nees and andrographolide in high-fructose-fat-fed rats. Indian journal of pharmacology. 2012.
- [89] Lakshmi V, Mahdi AA, Mishra V, Sharma D, Agarwal SK. antidiabetic activity in the leaves of *andrographis paniculata*.
- [90] Akbarsha MA, Murugaian P. Aspects of the male reproductive toxicity/male antifertility property of andrographolide in albino rats: effect on the testis and the cauda epididymidal spermatozoa. Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives. 2000.
- [91] Ahmad M, Mohammad N, Aziz MA, Alam MA, Hossain MS, Islam MR, Uddin MG. Comparison of antioxidant role of methanol, acetone and water extracts of *Andrographis paniculata* Nees. Journal of Medicinal Plants Research. 2020.
- [92] Verma N, Vinayak M. Antioxidant action of *Andrographis paniculata* on lymphoma. Molecular biology reports. 2008.
- [93] Hassan MM, Khan SA, Shaikat AH, Hossain E, Hoque A, Ullah H, Islam S. Analgesic and anti-inflammatory effects of ethanol extracted



- leaves of selected medicinal plants in animal model. *Veterinary World*. 2013.
- [94] Chang RS, Ding L, Gai-Qing C, Qi-Choa P, Ze-Lin Z, Smith KM. Dehydroandrographolide succinic acid monoester as an inhibitor against the human immunodeficiency virus. *Proceedings of the Society for Experimental Biology and Medicine*. 1991.
- [95] Gnanaiah S, RSA SK, Vincent A, Sangeetha m. isolation, purification & characterization of active compound from andrographis paniculata. I and testing its anti-venom and cytotoxic activity by in-vitro & in-vivo studies. *International Journal on Applied Bioengineering*. 2013.
- [96] Gupta S, Choudhry MA, Yadava JN, Srivastava V, Tandon JS. Antidiarrhoeal activity of diterpenes of *Andrographis paniculata* (Kal-Megh) against *Escherichia coli* enterotoxin in in vivo models. *International Journal of Crude Drug Research*. 1990.
- [97] Zhang YZ, Tang JZ, Zhang YJ. Study of *Andrographis paniculata* extracts on antiplatelet aggregation and release reaction and its mechanism. *Zhongguo Zhong xi yi jie he za zhi Zhongguo Zhongxiyi jiehe zazhi*= Chinese journal of integrated traditional and Western medicine. 1994.