WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 6.805
Volume 6, Issue 1, 270-286. Review Article ISSN 2277– 7105

REVIEW ON PHARMACOLOGICAL INVESTIGATION OF KARIYAT

Sachin Annasaheb Nitave*[1,2] and Dr. Kailasam Koumaravelou[1]

[1]PRIST University, Centre for Higher Learning & Research, Trichy – Thanjavur Highway, Thanjavur 613 403.

[2]Dr. J. J. Magdum Trust's Anil Alias Pintu Magdum Memorial Pharmacy College Dharangutti, Shirol, Kolhapur, Maharashtra, India.

Article Received on
03 Nov. 2016,

Revised on 24 Nov. 2016,
Accepted on 15 Dec. 2016

DOI: 10.20959/wjpr20171-7585

***Corresponding Author**
Sachin Annasaheb Nitave
Dr. J. J. Magdum Trust's Anil Alias Pintu Magdum Memorial Pharmacy College Dharangutti, Shirol, Kolhapur, Maharashtra, India.

ABSTRACT

Andrographis paniculata (*A. paniculata*) used in ancient oriental and ayurvedic medicine, commonly called as Kariyat belongs to the *Acanthaceae* family comprises of about 40 species. Only a few are popular for their use in folk medicine for assorted health concerns. Of these few, *A. paniculata* is the most important and it is extensively used in several medicinal systems such as Ayurvedha, Homeopathy, Naturopathy, Amchi, Modern, Unani and Siddha. In this review, various aspects of Kariyat such as morphology, cultivation & collection, phytoconstituents, pharmacological activities, safety and toxicity etc. are covered.

KEY WORDS: *Andrographis paniculata*, traditional uses, pharmacology.

INTRODUCTION

Nature has been a source of medicinal agents for thousands of years and since the beginning of mankind. Medicinal plant is an integral part of human life to combat the sufferings from the dawn of civilization. It is estimated that more than 80,000 of total plant species have been identified and used as medicinal plants around the world.[01] Over the past twenty years, interest in medicinal plants has grown enormously from the use of herbal products as natural cosmetics and for self-medication by the general public to the scientific investigations of plants for their biological effects in human beings.[02] Therefore, people are encouraging indigenous production and processing of these medicinal plants to use in different cultures and religion for the treatment of various diseases.[03]

One of such plant species is *Andrographis paniculata* (*A. paniculata*) used in ancient oriental and ayurvedic medicine. The genus *Andrographis* which belongs to the *Acanthaceae* family comprises of about 40 species. Only a few are popular for their use in folk medicine for assorted health concerns. Of these few, *A. paniculata* is the most important and it is extensively used in several medicinal systems such as Ayurvedha, Homeopathy, Naturopathy, Amchi, Modern, Unani and Siddha.[04]

A. paniculata is native to Tai- wan, Mainland China, Srilanka and India. It is also 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 Vietnam. This plant is also found in different phytogeographical and edaphic zones of China, America, West Indies and Christmas Island. *A. paniculata*, commonly known as King of Bitters or kalmegh.[05]

Taxonomic Hierarchy of *A. paniculata*

Taxonomic hierarchy is as follows[06]

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: Paniculata Nees

Morphology

Andrographis paniculata is an annual, branched, herbaceous plant grows erect to a height of 30– 110 cm in moist, shady places. The slender stem is dark green; shape squared in cross-

section with longitudinal furrows and wings along the angles having length 30–100cm and diameter 2–6mm and can be broken easily due to its fragile texture. The lance shaped leaves have hairless blades measuring up to 2–12 cm long and 1–3 cm wide with acute entire margin. The flowers possess calyx with 5 sepals which are small and linear. Corolla tubes are narrow, about 6 mm long, bilabiate, upper lip oblong, white with a yellowish top, whereas the lower tips are broadly cuneate, 3-lobed, white with violet markings. Stamens 2, inserted in the throat, anther basally bearded. Ovary superior, 2-celled with exerted style. Capsule of the herb is erect, linear-oblong, 1-2 cm long, compressed, longitudinally furrowed on broad faces with thin glandular hairs. The fruit is a capsule around 2 cm long and a few millimeters wide. It contains many yellow brown small seeds. It is also known as Bhui-neem, meaning "neem of the ground", since the plant, though being a small annual herb, has a similar strong bitter taste as that of the large Neem tree. The morphological data is presented in Figure 1 & Figure 2 indicates different stages of life cycle of crop of *Andrographis paniculata*.[07]

(a) Mature *A. paniculata*

(b) Flower *A. paniculata*

(c) Seeds *A. paniculata*

(d) Stem of *A. paniculata*

Figure 1: Morphology of *Andrographis paniculata*.

Sample A-30 days

Sample B - 60 days

Sample C - 90 days

Sample D-130 days (At maturity of the crop i.e. bearing flowers, fully matured seed capsules etc.)

Fig. 2 Different stages of life cycle of crop of *Andrographis paniculata* from 30 days to maturity of crop

Cultivation & Collection / Agronomic Techniques

A. paniculata is an annual, branched, erect, and herbaceous plant which grows in hedgerows throughout the plane lands, hill slopes, waste ground, farms, moist habitat, seashores and roadsides. It is cultivated in rainy season as Kharif crop in India. It also can be cultivated in garden. Moist shady places, forests and wastelands are preferable for their well development. Plants conventionally grow via seed culture. Planting and harvesting time has influenced the yield of plant. Usually, may to july is the recommended time for sowing *A. paniculata* seeds with a spacing of 30 × 15cm. However, seed dormancy is a major constrain in *A. paniculata* cultivation commercially. Although hormonal media and hot water treatment have been suggested to overcome this problem. This technique is not enough to meet the commercial quantities required due to variability among the seed-derived progenies and scanty and delayed rooting of seedlings. Therefore, nonconventional propagation methods such as plant

tissue culture techniques are alternative methods to produce plenty of plantlets within a short time and improve phytochemical contents in *A. paniculata*. Tissue culture techniques have been applied for large scale propagation of *A. paniculata*.[08] Flowering of the plants begins with the onset of monsoon. The plant grows luxuriantly with the moderation in temperature after end of monsoon. Maximum herb yield can be obtained in 90-100 days after which leaves begins to shed. The crop keeps dormant in winter. At the time of flowering, the active principle andrographolide is maximum in leaves. Since, the whole plant consists of active principals, plant material is dried in shade and powdered. A well protected crop grown during monsoon season yields 3.5 to 4 tones/ha of dried plant.

List of vernacular names of *A. paniculata*

Generally, the tree is known as "King of Bitters" for its extremely bitter taste. This plant has different names in different languages. The vernacular names of *A. paniculata* are presented as bellow. In addition, local people easily recognize plant species with vernacular names instead of binomial names.[09]

The vernacular names of *A. paniculata*

Sr. No.	Language	Name
01	Arabic	Quasabhuva
02	Assamese	Chiorta, Kalmegh
03	Azerbaijani	Acılar Sahı, Acılar Xanı (khanı)
04	Bengali	Kalmegh
05	Burmese	Se-ga-gyi
06	Chinese	Chuan Xin Lian
07	English	The Creat, King of Bitters
08	French	Chirette verte, Roi des amers
09	Gujarati	Kariyatu
10	Hindi	Kirayat, Kalpanath
11	Indonesian	Sambiroto, Sambiloto
12	Japanese	Senshinren
13	Kannada	Nelaberu
14	Konkani	Vhadlem Kiratyem
15	Lao	La-Sa-Bee
16	Malay	Hempedu Bumi, Sambiloto
17	Malayalam	Nelavepu, Kiriyattu
18	Manipuri	Vubati
19	Marathi	Oli-kiryata, Kalpa
20	Mizo	Hnakhapui
21	Oriya	Bhuinimba
22	Panjabi	Chooraita
23	Persian	Nain-e Havandi
24	Philippines	Aluy, Lekha and Sinta

25	Russian	Andrografis
26	Sanskrit	Kalmegha, Bhunimba and Yavatikta
27	Scandinavian	Green Chiratta
28	Sinhalese	Hın Kohomba or Heen Kohomba
29	Spanish	Andrografis
30	Tamil	Siriyanangai
31	Telugu	Nilavembu
32	Thai	Fa-Talai-Jorn, Fah-talai-jon (jone)
33	Turkish	Acılar Kralı, Acı Pa¸sa, Acı Bey
34	Urdu	Kalmegh, Kariyat, Mahatita
35	Vietnamese	Xuyen Tam Lien

Phytoconstituents

Medicinal plants contain physiologically active principles that over the years have been exploited in traditional medicine for the treatment of various ailments. *A. paniculata* contains diterpenes, lactones and flavonoids. Flavonoids mainly exist in the root, but have also been isolated from the leaves. The aerial parts contain alkanes, ketones and aldehydes. Although it was initially thought that the bitter substance in the leaves was the lactone andrographolide, later investigations showed that the leaves contained two bitter principles – andrographolide and a compound named kalmeghin. Four lactones – chuanxinlian A (deoxyandrographolide), B (andrographolide), C (neoandrographolide) and D (14-deoxy-11, 12-didehydroandrographolide) – were isolated from the aerial parts in China. A diterpene glucoside (deoxyandrographolide- 19beta-D-glucoside) has been detected in the leaves and six diterpenoids of the ent-labdane type, two diterpene glucosides and four diterpene dimers (bis-andrographolides A, B, C and D) have been isolated from aerial parts. Two flavonoids identified as 5,7,2',3'-tetramethoxyflavanone and 5-hydroxy-7,2',3'-trimethoxyflavone were isolated from the whole plant, while 12 new flavonoids and 14 diterpenoids have been reported from the aerial parts. Two new flavonoid glycosides and a new diterpenoid (andrographic acid) were recently reported and two new ent-labdane diterpenoid glycosides were isolated from the aerial parts.[10,11,12,13,14,15,16,17,18,19,20,21]

Pharmacological Investigation

Research conducted in the 90's has confirmed that *A. paniculata*, properly administered, has a surprisingly broad range of pharmacological effects, some of them extremely beneficial. The strong use of the different parts of *A. paniculata* plant in folk medicine, especially, in Asia lead scientists to study its pharmacological properties to validate its use as a therapeutic agent in the medicine of various ailments. Several studies showed that this plant exhibited various biological activities.

A. paniculata has been reported as having antibacterial, antifungal, antiviral, antimicrobial, hepatoprotective, antimalarial, cholerectic, hypoglycemic, hypocholesterolemic, adaptogenic, aperient, anti-inflammatory, emollient, astringent, diuretic, emmenagogue, gastric & liver tonic, carminative, anthelmintic activity. Due to its "blood purifying" action it is suggested for use in cases of leprosy, gonorrhea, scabies, boils, skin eruptions, chronic and seasonal fevers. *A. paniculata* is also used for the treatment of pharyngolaryngitis, diarrhea, dysentery, cough with thick sputum, carbuncle, sores and snake bites.

Hepatoprotective effects: *A. paniculata* is an component in a number of polyherbal preparations used as hepatoprotectants in India, one of which has been reported as effective in chronic hepatitis B virus infection. Very small number of studies on the effects of crude extracts of *A. paniculata* on liver functions is available. Most studies for hepatic effects have been conducted on either andrographolide or other purportedly active principles. The protection of andrographolide against acetaminophen-induced reduction in volume and contents of bile was better than that produced by silymarin. Multiple-dose pretreatment with arabinogalactan proteins and andrographolide was protective against ethanol induced hepatotoxicity in mice and was deemed comparable to the efficacy of silymarin.[22,23,24,25,26,27,28,29]

Antimicrobial and Antiparasitic Effects: *A. paniculata* has been extensively used to treat a variety of conditions of infectious origin in traditional systems of medicine. Modern research has investigated it for activity against various bacteria, viruses and parasites. Crude powder suspended in water was reported to be devoid of in vitro antibacterial activity against *Salmonella, Shigella, Escherichia coli, gram A Streptococcus* and *Staphylococcus aureus*, even at a concentration of 25 mg/mL crude powder. Andrographolide, neoandrographolide and 14-deoxy-11,12-didehydroandrographolide are reported to be viricidal against herpes simplex virus 1 (HSV-1) without having any significant cytotoxicity at viricidal concentrations. The chloroform extract completely inhibited malarial parasitic growth within 24 hours of incubation at a concentration of 0.05 mg/mL.[30,31,32,33,34,35,36,37,38,39]

Cardiovascular Effects: Aqueous extract of *A. paniculata* produced a dose-dependent fall in systolic blood pressure of both spontaneously hypertensive rats (SHRs) and normotensive Wistar-Kyoto rats, with a corresponding significant decrease in plasma angiotensin converting enzyme (ACE) activity and lipid peroxidation in kidneys in extract-treated SHRs. The decrease in ACE activity and lipid peroxidation were not significantly altered in

normotensive Wistar-Kyoto rats, an indication that suggests its hypotensive effect in hypertensive and normotensive rats is not mediated through identical mechanisms. The hypotensive effect of n-butanol and aqueous fractions of the crude water extract is antagonized by phentolamine, hexamethonium, pyrilamine and cimetidine, but not by propranolol, atropine or captopril. However, the fall in mean arterial pressure produced by 14-deoxy-11, 12-didehydroandrographolide (DDA), one of the three active diterpenoids, in anesthetized Sprague-Dawley rats was attenuated in the presence of propranolol, hexamethonium and captopril.[40,41,42]

Antioxidant and Anti-inflammatory Activities

Antioxidant and anti-inflammatory activities of *A. paniculata* and its constituents have been reported by various investigators. Studies reported that nicotine-induced inhibition of mitochondrial electron chain complexes and the resultant increase in nitric oxide (NO) in different parts of rats brains was prevented by simultaneous treatment with the water and ethanol extracts of *A. paniculata* or andrographolide; the water extract exhibited greater antioxidant activity than the ethanol extract. Phytochemical analysis showed higher flavonoid but lower phenol contents in water extract than in ethanol extract.[43,44,45,46,47,48,49,50,51,52]

Antifertility effect: A number of animal studies report an effect of *A. paniculata* on male and female reproduction. Early reports of oral administration of powdered stem indicated an antifertility effect in male Wistar mice, but no impact on fertility in female mice. It has also been reported that administration of *A. paniculata* resulted in abortion in pregnant rabbits. Intraperitoneal injection of the decoction of aerial parts to female albino mice was reported to prevent implantation and caused abortion at different gestation periods. Early pregnancy was also terminated by intramuscular, subcutaneous and intravenous administration. Existing evidence is too inconsistent, with some findings directly contradicting others, to reach any definitive conclusion about the reproductive effects of *A. paniculata*. The existing evidence does suggest that *A. paniculata* is unlikely to be an effective form of birth control. Further studies on short and long-term effects on fertility are necessary.[53,54,55]

Effect on Respiratory System

A. paniculata has been used for uncomplicated upper respiratory tract infections (URTIs). Pills (made from the whole powdered plant with water) and tablets (made from the water extract of the herb) are effective in URTI. *A. paniculata* is commonly used for the prevention

and treatment of common cold in several communities. A double-blind, placebo-controlled study of 61 adult patients suffering from common cold used Kan Jang tablets (made from *A. paniculata* dried extract) for 5 days. Within the treatment period, significant clinical improvement was observed on day 4 for 1200mg extract daily. Both groups showed significant reductions in clinical symptoms like shivering, sore throat, tiredness, muscular ache, rhinitis, sinus pains and headache.[56,57,58,59]

Antihyperglycemic / Hypoglycemic Effects

Water extract of *A. paniculata* significantly prevents orally administered glucose-induced hyperglycemia in nondiabetic rabbits without affecting epinephrine-induced hyperglycemia. Chronic administration of the extract for six weeks also showed no effect on fasting blood glucose level. However, ethanol extract, administered orally twice daily for 14 days to streptozotocin-induced diabetic rats significantly reduced fasting serum glucose and increased body weight in a dose-dependent manner.[60,61,62,63,64]

Anticancer: Andrographolide exhibited both direct and indirect effects on cancer cells by inhibiting proliferation of cancer cells, cell-cycle arrests or cell differentiation, enhancing body's own immune system against cancer cells; and inducting apoptosis and necrosis of cancer cells. Dichloromethane fraction of methanol extract significantly inhibited the proliferation of HT-29 colon cancer cells. The major bioactive compound of *A. paniculata* is andrographolide, isolated from dichloromethane inhibited the growth of a diverse cancer cell representing different types of human cancers.[65,66,67,68,69,70,71]

Anti-diarrhoeal and intestinal effects: Experiments in animals demonstrate that *A. paniculata* can prevent diarrhea. Extracts of *A. paniculata* had effectively shown activity against the diarrhea connected with E. coli infections. The *A. paniculata* components, Andrographolide and neoandrographolide showed comparable activity to loperamide (Imodium), the most common antidiarrhea drug. Gupta et al. reported that the active ingredients against diarrhoea are Andrographolide and deoxyandrographolide.[72,73]

Immunomodulatory activity: Intra-gastric administration of ethanol extracts of the stems and leaves (25 mg/kg bodyweight) or purified andrographolides (1 mg/kg bodyweight) to mice was reported to stimulate antibody production and the delayed-type hypersensitivity response to sheep red blood cells. The extract and purified andrographolide was also reported to stimulate an natural immune response in mice, measured by macrophage migration index,

phagocytosis of [14C] leucine-labelled E.coli and proliferation of splenic lymphocytes stimulated with *A. paniculata* extract.[74]

Safety and Toxicity Effects

Generally, uses of *A. paniculata* as a medicine have been proved to be safe in various studies on mice, rats and rabbits as well as in in-vitro assays and some clinical trials. Some conflicting results are also available. Due to *A. paniculata*'s extreme bitterness, it may cause emesis. Some adverse effects including allergic reaction, gastric instability, fatigue, headache, loss of appetite, lymphadenopathy, diarrhea, metallic taste and nausea are also observed in overdosing of *A. paniculata* extracts. It is suggested to avoid this plant during pregnancy due to its ovulation preventive effects. Few studies showed the toxic effect of *A. paniculata* on reproductive system by damaging the Sertoli cell in male gonads in albino rats.[75]

To date, all trials with few exceptions were for short duration; thus the prediction of safety for long term use would be farfetched.

CONCLUSION

A. paniculata has been extensively used as traditional medicine in India, China and Southeast Asia. The aerial parts possess most of the medicinal properties. From the vast literature study and experimental results analysis it can be concluded that *Andrographis paniculata* is widely cultivated and the demand of *Andrographis paniculata* is greatly increased in the past few years for its overwhelming therapeutic potentials. Its importance as a medicinal plant is growing up with stronger reports in support of its multifarious therapeutic uses. Available data on *Andrographis paniculata* also clearly expresses a broad spectrum of pharmacological properties of this plant. Taking great concern of the useful benefits of the plant, it can be advocated as a safe, highly important medicinal plant for mankind.

ACKNOWLEDGEMENT

I am thankful to Honorable Mr. Veejhay J. Magdum, Chairman Dr. J. J. Magdum trust, Jaysingpur.

REFERENCES

1. MEENU SHARMA and R. G. SHARMA, Identification, Purification and Quantification of Andrographolide from Andrographis Paniculata (Burma. F.) Nees By Hptlc At

Different Stages Of Life Cycle Of Crop J. Curr. Chem. Pharm. Sc., 2013; 3(23): ISSN 2277-2871.

2. Joseph Joselin and Solomon Jeeva, Andrographis paniculata: A Review of its Traditional Uses, Phytochemistry and Pharmacology, Joselin and Jeeva, Med Aromat Plants, 2014; 3: 4.
3. Agbonlahor Okhuarobo, Joyce Ehizogie Falodun, Osayemwenre Erharuyi, Vincent Imieje, Abiodun Falodun, Peter Langer, Harnessing the medicinal properties of Andrographis paniculata for diseases and beyond: a review of its phytochemistry and pharmacology, Asian Pac J Trop Dis 2014; 4: 213.
4. N. Karmegam, R. Nagaraj, S. Karuppusamy and M. Prakash, Biological and Pharmacological Activities of Andrographis spp. (Acanthaceae) Distributed in Southern Eastern Ghats, India, International Journal of Current Research in Biosciences and Plant Biology ISSN: 2349-8080 Volume 2 (September-2015),140.
5. Anil Kumar, Jyotsna Dora, Anup Singh and Rishikant Tripathi, A REVIEW ON KING OF BITTER (KALMEGH), IJRPC, 2 (2012), ISSN: 2231-2781.
6. Manoharan Sivananthan, Manoharan Elamaran, Medicinal and pharmacological properties of Andrographis paniculata, International Journal of Biomolecules and Biomedicine (IJBB) 2003; 3(1): ISSN: 2221-1063.
7. Deni Brown, *Encylopedia of Herbs*, Dorling Kindersley Limited Copyright ©: 1995; 2001, 120.
8. Md. Sanower Hossain, Zannat Urbi, Abubakar Sule, and K. M. Hafizur Rahman, Andrographis paniculata (Burm. f.) Wall. ex Nees: A Review of Ethnobotany, Phytochemistry, and Pharmacology, The Scientific World Journal 2014; Article ID 274905, 01.
9. Thanasekaran Jayakumar, Cheng-Ying Hsieh, Jie-Jen Lee,1,3,4 and Joen-Rong Sheu, Experimental and Clinical Pharmacology of Andrographis paniculata and Its Major Bioactive Phytoconstituent Andrographolide, Hindawi Publishing Corporation Evidence-Based Complementary and Alternative Medicine 2013; Article ID 846740, 01.
10. Priyanka Das, Alok Kumar Srivastav, Phytochemical Extraction and Characterization of the Leaves of Andrographis Paniculata for Its Anti- Bacterial, Anti-Oxidant, Anti-Pyretic and Anti- Diabetic Activity, International Journal of Innovative Research in Science, Engineering and Technology (An ISO 3297: 2007 Certified Organization) 2014; 15176.
11. Goodman, S., L., and Gilman, A. The Pharmacological Basis of Therapeutics, IX edition-Macmillan Publishing Co Inc, New York: 2000, 959

12. O. Sareer, A. Ahad, and S. Umar, "Prophylactic and lenitive effects of Andrographis paniculata against common human ailments: an exhaustive and comprehensive reappraisal," Journal of Pharmaceutical Research and Opinion, 2012; 2: 138.
13. D. Anju, G. Jugnu, S. Kavitha, N. Arjun, and D. Sandeep, "A review on medicinal prospective of Andrographis paniculata Nees," Journal of Pharmaceutical and Scientific Innovation, 2012; 1(1).
14. X. Q. Zhang, G. C. Wang, W. C. Ye, Q. Li, G. X. Zhou, and X. S. Yao, "New diterpenoids from Andrographis paniculata (Burm. f.) Nees," Journal of Integrative Plant Biology, 2006; 48: 1122.
15. Chen LX, Qu GX, Qiu F. Studies on flavonoids of Andrographis paniculata. Zhongguo Zhong Yao Za Zhi, 2006; 31: 391. [Article in Chinese]
16. Chen LX, Qu GX, Qiu F. Studies on diterpenoids from Andrographis paniculata. Zhongguo Zhong Yao Za Zhi, 2006; 31: 1594.[Article in Chinese]
17. Li W, Xu X, Zhang H, et al. Secondary metabolites from Andrographis paniculata. Chem Pharm Bull (Tokyo) 2007; 55: 455.
18. Zhou KL, Chen LX, Zhuang YL. et al. Two new ent-labdane diterpenoid glycosides from the aerial parts of Andrographis paniculata. J Asian Nat Prod Res 2008; 10: 939.
19. Li J, Huang W, Zhang H, Wang X and Zhou H: Synthesis of andrographolide derivatives and their TNF-alpha and IL-6 expression inhibitory activities. Bioorganic and Medicinal Chemistry Letters 2007; 17: 6891.
20. G. DEORA ANDROGRAPHIS PANICULATA- A REVIEW ON THE BIOLOGICAL ACTIVITIES OF THE PLANT IJPRBS, 2014; 3: 263.
21. Payal Chawla & et al., Review on King of Bitters: Andrographis paniculata, Asian Journal of Pharmaceutical Technology & Innovation, 2015; 03: 50.
22. Rajkumar JS, Sekar MG, Mitra SK. Safety and efficacy of oral HD-03/ES given for six months in patients with chronic hepatitis B virus infection. World J Gastroenterol 2007; 13: 4103.
23. D. N. Roy, S. Mandal, G. Sen, S. Mukhopadhyay, and T. Biswas, "14-Deoxyandrographolide desensitizes hepatocytes to tumour necrosis factor alpha induced apoptosis through calcium dependent tumour necrosis factor receptor super family member 1A release via the NO/cGMP pathway," British Journal of Pharmacology, 2010; 60: 1823.

24. G. A. Akowuah, I. Zhari, A. Mariam, and M. F. Yam, "Absorption of andrographolides from Andrographis paniculata and its effect on CCl4-induced oxidative stress in rats," Food and Chemical Toxicology, 2009; 47: 2321.
25. V. K. Verma, K. K. Sarwa, A. Kumar, and M. Zaman, "Comparison of hepatoprotective activity of Swertia chirayita and Andrographis paniculata plant of North-East India against CCl 4 induced hepatotoxic rats," Journal of Pharmacy Research, 2013; 7: 653.
26. Behera PR, Nayak P, Baric DP, Rautray TR, Thirunavoukkarasu M, Chand PK. ED-XRF spectrometric analysis of comparative elemental composition of in vivo and in vitro roots of Andrographis paniculatata (Burm.f.) Wall. ex Nees-a multi- medicinal herb. Appl Radiat Isot 2010; 68: 2229.
27. G. Shi, Z. Zhang, R. Zhang et al., "Protective effect of andrographolide against concanavalin A-induced liver injury," Naunyn's Schmiedebergs Archives of Pharmacology, 2012; 385: 69.
28. R. M. Kunwar, K. P. Shrestha, and R. W. Bussmann, "Traditional herbal medicine in far-west Nepal: a pharmacological appraisal," Journal of Ethnobiology and Ethnomedicine, 2010; 6: 1.
29. Pekthong D, Martin H, Abadie C, Bonet A, Heyd B, Mantion G and Richert L: Differential inhibition of rat and human cytochrome P450 by Andrographis paniculata extract and andrographolide. Journal of Ethnopharmacology, 2008; 115: 432.
30. Y. Padma, C. L. Narasimhudu, S. Devi, N. M. B. Natha, R. B. Naga, and G. H. Philip, "In vitro anthelmintic activity of Andrographis paniculata (burm.f.) nees," International Journal of Pharmaceutical Research and Developement, 2011; 3: 202.
31. Manjusha G, Rajathi K, Mini Alphonse JK, Meera K, Antioxidant potential and antimicrobial activity of Andrographis paniculata and Tinospora cordifolia against pathogenic organisms. Journal of Pharmacy Research 2011; 4: 452.
32. Radha R, Sermakkani M, Thangapandian V, Evaluation of phytochemical and antimicrobial activity of Andrographis paniculata nees (Acanthaceae) aerial parts. IJPLS 2011; 2: 562.
33. Abubacker MN, Vasantha S, Antibacterial activity of ethanolic leaf extracts of Andrographis paniculata Nees (Acanthaceae) and its bioactive compound Andrographolide. Drug invention today, 2010; 2: 440.
34. Chakraborty S, Biswas S, Sarkar Manna J, Das S, Dey R Sol-gel derived silica-gel as a controlled delivery system of Andrographis paniculata extract and its anti-microbial efficacy. Transactions of the Indian Institute of Metals, 2011; 64: 189.

35. Hosamani P, Lakshman HC, Sandeep Kumar K, Rashmi C, Hosamani D Antimicrobial Activity of Leaf extract of Andrographis paniculata Wall. Science Research Reporter, 2011; 1: 9.
36. Shihabudeen MS, Hansi Priscilla H, Kavitha Thirumurugan D (2010) Antimicrobial activity and phytochemical analysis of selected Indian folk medicinal plants. International Journal of Pharma Sciences and Research (IJPSR), 2010; 1: 430.
37. Sukesh K., Shafi T., Densingh J. Phytochemical investigation and antibacterial activity of Gymnemasylvestre and Andrographis paniculatafrom western ghats. Int. J. Phytomedicine, 2011; 3: 254.
38. S. Seubsasana, C. Pientong, T. Ekalaksananan, S. Thongchai, and C. Aromdee, "A potential andrographolide analogue against the replication of herpes simplex virus type 1 in vero cells," Medicinal Chemistry, 2011; 7: 237.
39. L. I. C. Tang, A. P. K. Ling, R. Y. Koh, S. M. Chye, and K. G. L. Voon,"Screening of anti-dengue activity in methanolic extracts of medicinal plants," BMC Complementary and Alternative Medicine, 2012; 12: 1.
40. P. Thisoda, N. Rangkadilok, N. Pholphana, L. Worasuttayan- gkurn, S. Ruchirawat, and J. Satayavivad, "Inhibitory effect of Andrographis paniculata extract and its active diterpenoids on platelet aggregation," European Journal of Pharmacology, 2006; 553: 39.
41. A. Y. H. Woo, M. M. Y. Waye, S. K. W. Tsui, S. T. W. Yeung, and C. H. K. Cheng, "Andrographolide up-regulates cellular- reduced glutathione level and protects cardiomyocytes against hypoxia/reoxygenation injury,". The Journal of Pharmacology and Experimental Therapeutics, 2008; 325: 226.
42. K. Awang, N. H. Abdullah, A. H. Hadi, and Y. S. Fong, "Car- diovascular activity of labdane diterpenes from Andrographis paniculata in isolated rat hearts," Journal of Biomedicine and Biotechnology, 2012 (2012), Article ID 876458, 01.
43. Das S, Gautam N, Dey SK, et al. Oxidative stress in the brain of nicotine-induced toxicity: protective role of Andrographis paniculata Nees and vitamin E. Appl Physiol Nutr Metab, 2009; 34: 124.
44. W.-F. Chiou, C.-F. Chen, and J.-J. Lin, "Mechanisms of suppres- sion of inducible nitric oxide synthase (iNOS) expression in RAW 264.7 cells by andrographolide," British Journal of Pharmacology, 2000; 129: 1553.
45. K. Sheeja, P. K. Shihab, and G. Kuttan, "Antioxidant and anti- inflammatory activities of the plant Andrographis paniculata nees," Immunopharmacology and Immunotoxicology, 2006; 28: 129.

46. Z. Bao, S. Guan, C. Cheng et al., "A novel antiinflammatory role for andrographolide in asthma via inhibition of the nuclear factor-κb pathway," The American Journal of Respiratory and Critical Care Medicine, 2009; 179: 657.
47. J. Liu, Z.-T. Wang, L.-L. Ji, and B.-X. Ge, "Inhibitory effects of neoandrographolide on nitric oxide and prostaglandin E2 production in LPS-stimulated murine macrophage," Molecular and Cellular Biochemistry, 2007; 298: 49.
48. A. A. Abu-Ghefreh, H. Canatan, and C. I. Ezeamuzie, "In vitro and in vivo anti-inflammatory effects of andrographolide," International Immunopharmacology, 2009; 9: 313.
49. Parichatikanond W, Suthisisang C, Dhepakson P, Herunsalee A. Study of anti-inflammatory activities of the pure compounds from Andrographis paniculata (Burm.f.) Nees and their effects on gene expression. Int Immunopharmacol, 2010; 10: 1361.
50. Chao WW, Kuo YH, Hsieh SL Lin BF. Inhibitory effects of ethyl acetate extract of Andrographis paniculata on NF-kB trans-activation activity and LPS-induced acute inflammation in mice. Evid Based Complement Alternat Med 2011; 254531.
51. 51. Lin FL, Wu SJ, Lee SC, Ng LT. Antioxidant, antioedema and analgesic activities of Andrographis paniculata extracts and their active constituent andrographolide. Phytother Res, 2009; 23: 958.
52. Verma N, Vinayak M. Antioxidant action of Andrographis paniculata on lymphoma. Mol Biol Rep 2008; 35: 535.
53. R. Kamal, R. S. Gupta, and N. K. Lohiya, "Plants fo rmale fertility regulation," Phytotherapy Research, 2003; 17: 579.
54. M. A. Akbarsha and P. Murugaian, "Aspects of the male reproductive toxicity/male antifertility property of andrographolide in albino rats: effect on the testis and the cauda epididymidal spermatozoa," Phytother Research, 2000; 14: 432.
55. J. Sattayasai, S. Srisuwan, T. Arkaravichien, and C. Aromdee, "Effects of andrographolide on sexual functions, vascular reactivity and serum testosterone level in rodents," Food and Chemical Toxicology, 2010; 48: 1934.
56. Coon JT, Ernst E. Andrographis paniculata in the treatment of upper respiratory tract infections: A systematic review of safety and efficacy. Planta Med, 2004; 70: 293.
57. *Poolsup* N, Suthisisang C, Prathanturarug S, Asawamekin A, Chanchareon U. Andrographis paniculata in the symptomatic treatment of uncomplicated upper respiratory tract infection: Systematic review of randomized controlled trials. J Clin Pharm Ther 2004; 29: 37.

58. Gabrielian ES, Shukarian AK, Goukasova GI, Chandanian GL, Panossian AG, Wikman G, A double blind, placebo-controlled study of Andrographis paniculata fixed combination Kan Jang in the treatment of acute upper respiratory tract infections including sinusitis. Phytomedicine 2002; 9: 589.
59. N. Poolsup, C. Suthisisang, S. Prathanturarug, A. Asawamekin, and U. Chanchareon, "Andrographis paniculata in the symptomatic treatment of uncomplicated upper respiratory tract infection: systematic review of randomized controlled trials," Journal of Clinical Pharmacy and Therapeutics, 2004; 29: 37.
60. B. C. Yu, C. K. Chang, C. F. Su, and J. T. Cheng, "Mediation of β-endorphin in andrographolide-induced plasma glucose- lowering action in type I diabetes-like animals," Naunyn- Schmiedeberg's Archives of Pharmacology, 2008; 377: 529.
61. R. Gupta, K. G. Bajpai, S. Johri, and A. M.Saxena, "An overview of Indian novel traditional medicinal plants with anti-diabetic potentials," African Journal of Traditional, Complementary and Alternative Medicines, 2008; 5: 1.
62. Z. Zhang, J. Jiang, P. Yu, X. Zeng, J. W. Larrick, and Y. Wang, "Hypoglycemic and beta cell protective effects of andrographolide analogue for diabetes treatment," Journal of Translational Medicine, 2009; 7: 62.
63. Umamaheswari S., Mainzen, Prince P.S,, Antihyperglycaemic effect of 'Ilogen-Excel', an ayurvedic herbal formulation in streptozotocin-induced diabetes mellitus, Acta Pol Pharm, 2007; 64: 53.
64. Subramanian R, Asmawi MZ and Sadikun A: In vitro alpha-glucosidase and alpha-amylase enzyme inhibitory effects of Andrographis paniculata extract and andrographolide. Acta Biochimica Polonica, 2008; 55: 391.
65. V. S. P. K. Aditya, N. L. Kumar, and A. Mokkapati, "Evaluation of in vitro cytotoxicity of Andrographis paniculata, Duranta serratifolia and Albizzia lebbeck whole plant extracts by MTT assay against MCF-7 and HT-29 cell lines," Current Research in Microbiology and Biotechnology, 2014; 2: 351.
66. M. Geethangili, Y. K. Rao, S.-H. Fang, and Y.-M. Tzeng, "Cyto- toxic constituents from Andrographis paniculata induce cell cycle arrest in Jurkat cells," Phytotherapy Research, 2008; 22: 1336.
67. S. R. Jada, G. S. Subur, C. Matthews et al., "Semisynthesis and in vitro anticancer activities of andrographolide analogues," Phytochemistry, 2007; 68: 904.

68. S. D. Manikam and J. Stanslas, "Andrographolide inhibits growth of acute promyelocytic leukaemia cells by inducing retinoic acid receptor-independent cell differentiation and apoptosis," The Journal of Pharmacy and Pharmacology, 2009; 61: 69.
69. C. G. Jiang, J. B. Li, F. R. Liu, T. Wu, M. Yu, and H. M. Xu, "Andrographolide inhibits the adhesion of gastric cancer cells to endothelial cells by blocking E-selectin expression," Anticancer Research, 2007; 27: 2439.
70. Kumar RA, Sridevi K, Kumar NV, Nanduri S, Rajagopal S. Anticancer and immunostimulatory compounds from Andrographis paniculata. J Ethnopharmacol 2004; 92: 291.
71. Cheung MT, Ramalingam R, Lau KK, Chiang WL and Chiu SK: Cell type-dependent effects of andrographolide on human cancer cell lines. Life Sciences 2012; 91: 751.
72. Sindermsuk J, The antibacterial activities of the pure extract compounds from Andrographis paniculata on predominate pathogenic enteric bacilli in Thailand. Department of Medical Service Bulletin 1993; 18: 394.
73. Duke JA, and Ayensu ES, Medicinal plants of China. Algonac: Reference Publication, Inc., *Michigan*, 1985; 705.
74. Puri A, Saxena R, Saxena RP, Saxena KC, Srivastava V, Immunostimulant agents from Andrographis paniculata. J Nat Prod, 1993; 56: 995.
75. Chandrasekaran CV, Thiyagarajan P, Sundarajan K, Goudar KS, Deepak M, Murali B, et al. Evaluation of the genotoxic potential and acute oral toxicity of standardized extract of Andrographis paniculata (Kalmcold). Food Chem Toxicol, 2009; 47: 1892.