

Ethnobotanical and Pharmacological activity of *Andrographis Paniculata*

¹Hossein Hassanpour Golshani, ²Dr Pravin Badhe

¹Student researcher, ²Associate professor

Pharmacology department

¹Sinhgad College of Pharmacy Vadgaon (B.K) Pune

²Swalife Biotech Ltd, Cork Ireland

Abstract– *Andrographis paniculata* is one of the highly used potential medicinal plants in the world. It has been used for the treatment of viral to chronic diseases, and as an antioxidant. All parts of this plant are used to extract the active phytochemicals, different secondary metabolites such as glycosides, saponins and terpenoids play important role in the activity.

In this review, we have discussed its botanical, geographical and pharmacology specially plant extracts and major constituents that have played important role in different diseases.

Index terms- *Andrographis Paniculata*; lead product; natural product; pharmacological activity; Immunomodulatory activity

I. Introduction

Medicinal plants are prevalent from the origin of the earth and have been efficiently used by ancient people as a treatment for various diseases [6]. The plant extracts are identified and act as an important source of the active ingredient and secondary metabolite products such as alkaloid, glycosides, saponins, tannins and terpenoids, which is used in therapeutic diseases, for drug production and for maintaining good health by both the traditional and orthodox medical practitioners [7,8].

II. Taxonomical classification of *Andrographis paniculata*:

Kingdom: Plantae, PlantsSub

Kingdom: Tracheobionta, Vascular plants;

Super Division : Spermatophyta, Seed plants;

Division: Angiosperma

Class: Dicotyledonae

Sub class: Gamopetalae

Series: Bicarpellatae

Order: Personales

Tribe: Justiciaeae

Family: Acanthaceae

Genus: *Andrographis*

Species: *A. paniculata*(Burm. f) Nees



(Fig. 1: *Andrographis paniculata* [4])

Andrographis Paniculata (Burm. F.) belongs to the family Acanthaceae. Mostly dried leaves and tender shoots are used in the study. The common name used is Kalmegh, Chirayita, Creat etc. in a different language.

Andrographis paniculata (Burm. F.) Wall. Ex Nees (AP) also called Kalmegh or "King of Bitters" belongs to family Acanthaceae[5]. It has been used for centuries in Asia to treat gastro-intestinal tract and upper respiratory infections, fever, herpes,

sore throat, and a variety of other chronic and infectious diseases[6,7]. It is an annual and branched plant with lanceolate green leaves and attains heights of 60-70 cm. It grows abundantly in Asian countries like India, Sri Lanka, Pakistan, Java, Malaysia and Indonesia and is one of the commonly used medicinal plants in Ayurvedic and Unani systems of medicines. The plant is also known as the 'king of bitters' because it is extremely bitter in taste in every part of plant body [8,9].

Andrographis paniculata (Nees), is a valuable traditional medicinal plant and it has many important bioactive compounds [10]. It cures and prevents a number of diseases in human beings. It cures a cold, fever, colic pain, active against inflammatory, antidiabetic activity, antioxidant, antifertility, cardiovascular and anti-virus including inhibited HIV [11].

III. BOTANICAL DESCRIPTION:

AP is an annual, branched, herbaceous plant erecting to a height of 30-110 cm in moist shady places with stem acutely quadrangular much-branched, easily broken fragile texture stem. Leaves are simple, opposite, lanceolate, glabrous, 2–12cm long, 1–3cm wide with margin acute and entire or slightly undulated and upper leaves often bractiform with a short petiole. Inflorescence of the plant is characterized as patent, terminal and axillary in panicle, 10–30 mm long; bract small; pedicel short [4,12].

The flowers possess botanical features of calyx 5-partite, 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 exerted; anther basally bearded. Superior ovary, 2-celled; style far exerted. The capsule of the plant is erect, linear-oblong, 1–2 cm long and 2–5 mm wide, compressed, longitudinally furrowed on broad faces, acute at both ends, and thinly glandular-hairy. Seeds are very small, subquadratic[12,13]

The current aim of this review is to accumulate the morphological and pharmacological applications of *Andrographis paniculata* as a multipurpose drug showing efficient activity in curing various diseases

IV. Geographical distribution:

The genus *Andrographis* is composed of roughly 40 species several members of which enjoy a reputation in traditional medicine[14]. AP populations are distributed over a broad eco-geographical range in tropical Asian countries often in isolated patches. It grows abundantly in Southern and Southeastern Asia, including India, Sri Lanka, Pakistan and Indonesia [15].

So-called "native populations" occur only in the Indian subcontinent and especially South India and Sri Lanka, which perhaps represent the centre of origin and diversity of the species [16,17], stated that the herb is an introduced species in the northern areas of India, Thailand, Brunei, Malaysia, Indonesia, the West Indies such as Jamaica, Barbados and Bahamas, Hong Kong and in the tropical areas of the Americas[15,17,18].

This plant is also currently cultivated in southwestern Nigeria [19]. AP can be stemmed in a variety of habitats, for instance; plains, hill slopes, wastelands, farms, dry or wetlands, seashores, and even roadsides, but it has a preferred tendency to grow in moist shady places, forests, and wastelands [15,17].

V. MORPHOLOGY OF ANDROGRAPHIS PANICULATA:

(Table No.1 Morphology of AP [20,21,22])

1.	Plant height	30–110 cm
2.	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
3.	Leaves	Glabrous
	Length	2–12 cm
	Width	1–3 cm
	Arrangement	Lanceolate
	Shape	Pinnate, acute apex, entire margin
4.	Flowers	White with rose-purple spots on the petals
	Size	Small, in lax spreading axillary and terminal racemes or panicles
5.	Seed	Capsules linear-oblong, acute at both ends
	Size	1.9 cm × 0.3 cm
	Color	Yellowish brown
	Shape	Subquadrate, numerous
6.	Flowering and fruiting	December to April

VI. Pharmacological activity of *Andrographis paniculata*:

A. paniculata's aerial parts, roots, and entire plant have been used as traditional medicine in Asia for ages to cure a variety of diseases [7]. Stomachaches, inflammation, pyrexia, and intermittent fevers have all been treated with it by traditional medical practitioners[8].

The entire plant has been used to treat dyspepsia, influenza, diarrhoea, malaria, and respiratory infections, as well as as an antidote for snake bites and toxic stings from some insects. Infectious sickness, fever-causing diseases, colic pain, loss of appetite, irregular faeces, and diarrhoea are all treated with the leaf extract. A decoction of the aerial portions is used to treat the common cold, hypertension, diabetes, cancer, malaria, and snake bites in Malaysia [9,10,23].

Pharmacological activity:

Anti-inflammation–

- i) LPS-induced NO production by suppressing iNOS.
- ii) Complement 5a-induced macrophage recruitment via ERK1/2 and PI3K signal pathways.
- iii) Binding of NF- κ B oligonucleotide to nuclear proteins via ERK1/2 or PI3/Akt signal pathway [23,24,25].

Anti-cancer–

- i) Proliferation of HL-60 cells, the JAK-STAT3 pathway.
- ii) Tumor suppressor p53 expression, MAPKs (p38 kinase, JNK, ERK1/2) signaling pathway.
- iii) oncogene v-Src protein expression and v-Src-induced transformation.
- iv) Tumor in melanoma subcutaneously implanted mice (orally 200, 400 mg/kg BW, 10d) [26,27,28].

Immunomodulation–

- i) Proliferation and IL-2 induction in hPBL.
- ii) antibody and the delayed-type hypersensitivity response (orally 1 mg/kg, 7d).
- iii) NF- κ B expression in lung and airway epithelial cells infiltration of inflammatory cells in lung, airway hyperreactivity (i.p. 2 μ g/g BW, 7d).
- iv) LPS induced dopaminergic neurodegeneration in primary rat mesencephalic neuron-glia cultures.
- v) IL-2 production, proliferation, antibody production, T cell activation in EAE (i.p. 4 mg/kg BW).
- vi) Symptom and immunological markers in patients with RA (30% andrographolide tablet, 14 weeks) [29,30,31].

Anti-infection-

HIV induced cell cycle dysregulation, CD4+lymphocyte levels in HIV-1 infected individuals viricidal activity against HSV-1, EBV, via producing mature virus particle [32].

Anti-hepatotoxicity-

- i) CYP1A1 and CYP1A2 mRNA in mouse hepatocytes, synergistic effect in with a CYP1A1 inducer.
- ii) Expression of the pi class of glutathione S-transferase [33,34].

Anti-atherosclerosis-

- i) HUVECs apoptosis via enhancement of PI3K-Akt activity.
- ii) Thrombin-induced platelet aggregation via ERK1/2 pathway [25,35].

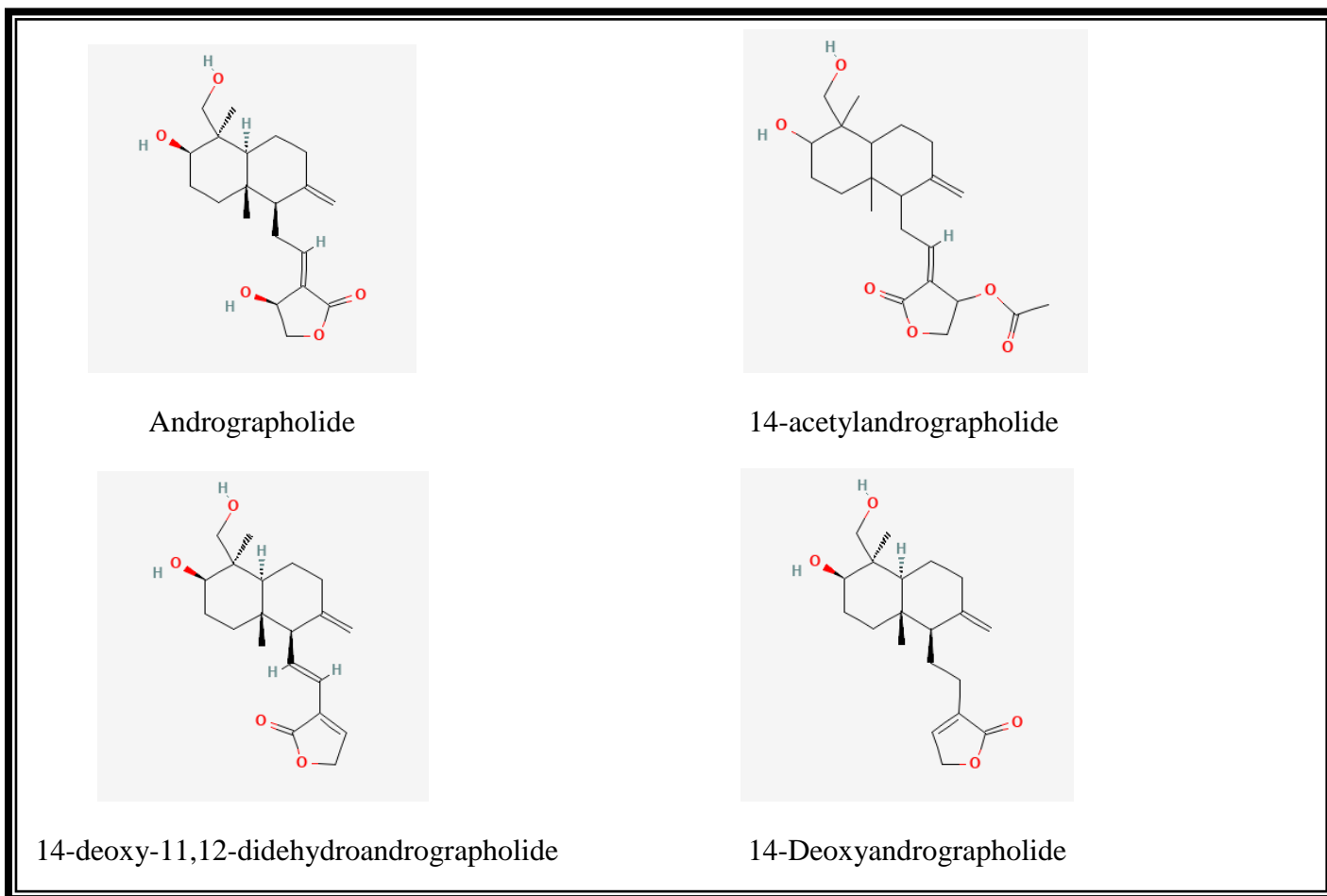
Anti-hyperglycemic effect-

- i) Plasma glucose concentrations of STZ-diabetic rats (oral 1.5 mg/Kg).
- ii) mRNA and protein levels of GLUT4 in soleus muscle [36,37].

Anti-Oxidation-

- i) MDA formation.
- ii) GSH, SOD activity [38].

VII. Chemical constituents and their pharmacological action:



(Fig No.2: Chemical Structures [39])

Andrographolides have shown anticancer, bioactivities & hepatoprotective. It has also been reported to suppress IL-2 production and T-cell proliferation in a mixed lymphocyte reaction and to inhibit dendritic cell maturation and antigen presentation [40,41]. The other chemical constituent is 14-deoxyandrographolide which helps in the activation of NOS and guanylatecyclasevaso relaxation *in vitro* and *in vivo*, enhanced proliferation and interleukin-2 induction in human peripheral blood lymphocytes [25,42,43].

Neoandrographolide: NO, PGE₂, iNOS and COX-2 in activated macrophages CCl₄, tBHP-induced hepatotoxicity (*i.p*100 mg/kg, 3d)[38,44]. 14-deoxy-11,12-didehydroandrographolide: Muscle relaxation, NO release from endothelial cells and anticancer[42,45]. 14-deoxy-14,15-didehydroandrographolide cytotoxic activity and cell cycle arrest of tumor cells NF- κ B-dependent trans-activation.[40]

Andrograpanin protein kinase or p38 MAPKs pathways chemokine SDF-1 α induced chemotaxis in Jurkat and THP-1 cells [35,46]. Isoandrographolide cell-differentiation-inducing activity proliferation of HL-60 cells [47,48]. 14-acetylandrographolide Growth of leukemia, ovarian, renal cancer cells [49]. 19-Oacetylanhydroandrographolide NF- κ B-dependent trans-activation[46]. Kalmeghin Fever & cold[50]. Andrographiside Anti-oxidant, anti-lipoxidant, carcinogenic & detoxification[51,52].

VIII. Conclusion-

A. paniculata has been shown to have consistent hepatoprotective effects. Furthermore, its incorporation in effective herbal extracts formulations for liver illnesses that are resistant to current treatment adds to its potential efficacy. Apart from this *A. paniculata* exhibits properties like Anti-oxidant, Cardiovascular effect, Anti-inflammatory, and Anti-Hyperglycemic properties. Some phytochemicals found in medicinal plants have been shown to have significant anti-mutagenic, and anti-carcinogenic properties, and their potential for cancer treatment and prevention. Further studies related to anti-cancer activity is being investigate.

REFERENCES:

1. Argal A and Pathak AK.J Ethnopharmacological .2006;106:142-145
2. Negi AS, Kumar JK , Luqman S, Sbanker K, Gupta MM and Kbanuja SPS. Med Res.2008;28(5):821
3. Hhang C J, W u MC .J.Biomed.Science,2008;9 :596-606
4. Liaqat H (2021) Andrographis paniculata: A Review of its Anti-Cancer Potential. Med Aromat Plants (Los Angeles) 18-May-2021, DOI: 10.35248/2167-0412.21.10.384

5. Negi AS, Kumar JK, Luqman S, Sbanker K, Gupta MM, Kbanuja SPS: Recent advances in plant hepatoprotectives: a chemical and biological profile of some important leads. *Med Res Rev.* 2008, 28 (5): 821-10.1002/med.20136.
6. Roxas M, Jurenka J: Colds and influenza: A review of diagnosis and conventional, botanical and nutritional considerations. *Altern Med Rev.* 2007, 12: 25-48.
7. Kligler B, Ulbricht C, Basch E, Kirkwood CD, Abrams TR, Miranda M, Singh Khalsa KP, Giles M, Boon H, Woods J: *Andrographis paniculata* for the treatment of upper respiratory infection: a systematic review by the natural standard research collaboration. *Explore.* 2006, 2 (1): 25-29. 10.1016/j.explore.2005.08.008.
8. Davi G, Falco A: Oxidant stress, inflammation and atherogenesis. *Lupus* 2005, 14:760-764.
9. O'Shea JJ, Murray PJ: Cytokine signaling modules in inflammatory responses. *Immunity* 2008, 28 (4):477-87.
10. K. Jarukamjorn and N. Nemoto, "Pharmacological aspects of *Andrographis paniculata* on health and its major diterpenoid constituent andrographolide," *Journal of Health Science*, vol. 54, no. 4, pp. 370–381, 2008.
11. Liu J, Wang ZT, Ji LL: *In vivo* and *in vitro* anti-inflammatory activities of Neoandrographolide. *Am J Chin Med* 2007, 35:317-328.
12. Thai Herbal Pharmacopoeia. Vol. 1. 1995. Bangkok, Prachachon Co.
13. Manual for cultivation, production and utilization of herbal medicines in primary healthcare. Nonthaburi, Department of Medical Sciences, Ministry of Public Health (1990).
14. Rao YK, Vimalamma G, Rao CV, Tzeng YM (2004) Flavonoids and andrographolides from *Andrographis paniculata*. *Phytochemistry* 65(16):2317–2321
15. Mishra SK, Sangwan NS, Sangwan RS (2007) *Andrographis paniculata* (Kalmegh): a review. *Phcog Rev* 1(2):283–298
16. Hooker JD (1885) The flora of British India, Vol. IV. p.501. Henrietta Street, Convent Garden, London
17. Bhat VS, Nanavati DD (1977) *Andrographis paniculata* (Burm. f.) Wall. ex Nees (kalmegh). *Indian Drugs* 15:187–190
18. Ridley HN (1925) The Flora of the Malay Peninsula, Vol V. The Flora of the Malay Peninsula, Vol V
19. Correll DS, Correll HB (1982) The flora of the bahama archipelago. J Cramer, Vaduz, Liechtenstein, p 1692
20. Fasola TR, Ayodele AE, Odetola AA, Umotok NE (2010) Foliar epidermal morphology and anti-diabetic property of *Andrographis paniculata* (Burm. f.) Wall ex. Nees. *Ethnobot Leaflets* 14:593–598
21. Mishra SK, Sangwan NS, Sangwan RS. *Andrographis paniculata* (Kalmegh): A review, *Pharmacognosy Reviews*, 2007; 1:283-298.
22. Kabeeruddin M, Kitabul Advia, 2, Aligarh Barqi Press, Delhi, 1937, 148-150.
23. Shahid A, *Andrographis paniculata*: A review of pharmacological activities and clinical effects, *Alternative Medicine Review*, 2011; 16:66-77
24. Xia YF, Ye BQ, Li YD, Wang JG, He XJ, Lin X: And rographolide attenuates inflammation by inhibition of NF- κ B activation through covalent modification of reduced cysteine 62 of p50. *J Immunol*2004, 173:4207-4217.
25. Chao WW, Kuo YH, Lin BF: Anti-inflammatory Activity of New Compounds from *Andrographis paniculata* by NF- κ B Trans-Activation inhibition. *J Agric Food Chem*2010, 58:2505-2512.
26. Chen JH, Hsiao G, Lee AR, Wu CC, Yen MH: Andrographolide suppresses endothelial cell apoptosis via activation of phosphatidyl inositol-3-kinase/Akt pathway. *Biochem Pharmacol* 2004, 67:1337-1345.
27. Rajagopal S, Kumar RA, Deevi DS, Satyanarayana C, Rajagopalan R: Andrographolide, a potential cancer therapeutic agent isolated from *Andrographispaniculata*. *J Exp Ther Oncol* 2003, 3:147-158.
28. Zhou J, Lu GD, Ong CS, Ong CN, Shen HM: Andrographolide sensitizes cancer cells to TRAIL-induced apoptosis via p53 mediated beath receptor 4 up-regulation. *Mol Cancer Ther*2008, 7 (7):2170-2180.
29. Yang L, Wu D, Luo K, Wu S, Wu P: Andrographolide enhances 5-fluorouracil induced apoptosis via caspase 8 dependent mitochondrial pathway involving p53 participation in hepatocellular carcinoma (SMMC-7721) cells. *Cancer Lett*2009, 276:180-188
30. Carretta MD, Alarcon P, Jara E, Solis L, Hancke JL, Concha II, Hidalgo MA, Burgos RA: Andrographolide reduces IL-2 production in T-cells by interfering with NFAT and MAPK activation. *Eur J Pharmacol*2009, 602:413-421.
31. Abu-Ghefreh AA, Canatan H, Ezeamuzie CI: *In vitro* and *in vivo* anti-inflammatory effects of andrographolide. *Int Immunopharmacol* 2009, 9:313-318.
32. Xu Y, Chen A, Fry S, Barrow RA, Marshall RL, Mukkur TKS: Modulation of immune response in mice immunized with an inactivated *Salmonella* vaccine and gavaged with *Andrographis paniculata* extract or andrographolide. *Int Immuno pharmacol* 2007, 7:515-5238
33. Calabrese C, Berman SH, Babish JG, Ma X, Shinto L, Dorr M, Well K, Wenner CA, Standish LJ: A phase I trial of andrographolide in HIV positive patients and normal volunteers. *Phytother Res* 2000, 14:333-338.
34. Jaruchotikamol A, Jarukamiorn K, Sirisangtrakul W, Sakuma T, Kawasaki Y, Nemoto N: Strong synergistic induction of CYP1A1 expression by and rographolide plus typical CYP1A inducers in mouse hepatocytes. *Toxicol Appl Pharmacol*2007, 224:156-162.
35. Chatuphonprasert W, Jarukamjorn K, Kondo S, Nemoto N: Synergistic increases of metabolism and oxidation reduction genes on their expression after combined treatment with a CYP1A inducer and andrographolide. *Chem Biol Interact* 2009, 182:233-238.
36. Thisoda P, Rangkadilok N, Pholphana N, Worasuttayangkurn L, Ruchirawat S, Satayavivad J: Inhibitory effect of *Andrographis paniculata* extract andits active diterpenoids on platelet aggregation. *Eur J Pharmacol* 2006, 553:39-45.
37. Yu BC, Hung CR, Chen WC, Cheng JT: Antihyperglycemic effect of andrographolide in streptozotocin induced diabetic rats. *Planta Med* 2003, 69:1075-1079.

38. Yu BC, Chang CK, Su CF, Cheng JT: Mediation of β -endorphin in and rographolide induced plasma glucose lowering action in type I diabetes like animals. *Naunyn-Schmiedeberg's Arch Pharmacol* 2008, 377:529-540.
39. Gulshan Kumar , Davinder Singh , Javeed Ahmad Tali , Divya Dheer , RaviS hankara : Chemical modification and its effect on biological activities , bioorganic-chemistry journal , January 2020, 103511
40. Kapil A, Koul IB, Banerjee SK, Gupta BD: Antihepatotoxic effects of major diterpenoid constituents of *Andrographis paniculata*. *Biochem Pharmacol* 1993, 46 (1):182-185.
41. Geethangili M, Rao YK, Fang SH, Tzeng YM: Cytotoxic constituents from *Andrographis paniculata* induce cell cycle arrest in Jurkat cells. *Phytother Res* 2008, 22:1336-1341
42. Chen L, Zhu H, Wang R, Zhou K, Jing Y, Qiu F: *ent*-Labdanediterpenoid lactone stereoisomers from *Andrographis paniculata*. *J Nat Prod* 2008, 71:852-855.
43. Zhang CY, Tan BK: Effects of 14-deoxyandrographolide and 14-deoxy-11,12-didehydroandrographolide on nitric oxide production in cultured human endothelial cells. *Phytother Res* 1999, 13:157-159
44. Burgos RA, Hancke JL, Bertoglio JC, Aguirre V, Arriagada S, Calvo M, Caceres DD: Efficacy of an *Andrographis paniculata* composition for the relief of rheumatoid arthritis symptoms: a prospective randomized placebo controlled trial. *Clin Rheumatol* 2009, 28:931-946.
45. Yooan N, Thisoda P, Rangkadilok N, Sahasitawat S, Pholphana N, Ruchirawat S: Cardiovascular effects of 14-deoxy-11,12-didehydroandrographolide and *Andrographis paniculata* extracts. *Planta Med* 2007, 73:503-511
46. Ji LL, Wang Z, Dong F, Zhang WB, Wang ZT: Andrograpanin, a compound isolated from anti-inflammatory traditional Chinese medicine *Andrographis paniculata*, enhances chemokine SDF-1 α -induced leukocytes chemotaxis. *J Cell Biochem* 2005, 95:970-978.
47. Chen L, Zhu H, Wang R, Zhou K, Jing Y, Qiu F: *ent*-Labdanediterpenoid lactone stereoisomers from *Andrographis paniculata*. *J Nat Prod* 2008, 71:852-855
48. Matsuda T, Kuroyanagi M, Sugiyama S, Umehara K, Ueno A, Nishi K: Cell differentiation inducing diterpenes from *Andrographis paniculata* Nees. *Chem Pharm Bull (Tokyo)* , 42:1216-1225.
49. Jada SR, Suseno GS, Matthews C, Hamzah AS, Lajis NH, Saad MS, Stevens MFG, Stanslas J: Semisynthesis and *in vitro* anticancer activities of andrographolide analogues. *Phytochemistry* 2007, 68:904-912.
50. Yang L, Wu D, Luo K, Wu S, Wu P: Andrographolide enhances 5-fluorouracil induced apoptosis via caspase 8 dependent mitochondrial pathway involving p53 participation in hepatocellular carcinoma (SMMC-7721) cells. *Cancer Lett* 2009, 276:180-188.
51. Liang FP, Lin CH, Kuo CD, Chao HP, Fu SL: Suppression of v-Src transformation by andrographolide via degradation of the v-Src protein and attenuation of the Erksignaling pathway. *J Biol Chem* 2008, 283 (8):5023-5033.
52. Shi MD, Lin HH, Chiang TA, Tsai LY, Tsai SM, Lee YC, Chen JH: Andrographolide could inhibit human colorectal carcinoma Lovo cells migration and invasion via down regulation of MMP-7 expression. *ChemBiol Interact* 2009, 180:344-352.