



# Insights Into Phyto Pharmaceutical, Pharmacological Properties Studies Of *Andrographis Paniculata*: A Review

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**ABSTRACT:** *Andrographis paniculata* (Burm f.) Nees is a medical plant that is widely utilized in diverse nations as a valued ancient herbal remedy. It contains numerous key bioactive elements and is an effective medication utilized in many formulations in Ayurveda, Siddha, and Homoeopathy. It treats and prevents a variety of ailments in humans and is a natural benefit to human health. This medicinal plant is extremely useful in the treatment of a variety of ailments, including malaria, diabetes, viral hepatitis, cirrhosis, and liver cancer. *Andrographis paniculata* (King of Bitters), also known as Kalmegh, belongs to the acanthaceae family, and its principal ingredients are diterpenoids, flavonoids, polyphenols, and other miscellaneous chemicals. The main components of andrographolides are 14-deoxy-12-methoxyandrographolide, 14-deoxy-11, 12-didehydroandrographolides, and 14-deoxyandrographolide.

This review discusses the past and current state of research on *Andrographis paniculata* in terms of medicinal usage, phytochemistry, pharmacological properties, and other aspects. This assessment is based on a review of the literature in scientific journals and books from libraries and online sources. The plant's extract and pure compounds have been reported to exhibit a range of activities, including antimicrobial, Antioxidant, Immunomodulatory Activity, Antipyretic and Analgesic, Antimalarial, Hepatoprotective, etc.

**KEY WORDS-** *Andrographis paniculate*, acanthaceae, Kalmegh, King of Bitters.

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## I. INTRODUCTION

The world is provided with an abundance of therapeutic plants. The sheer number and variety of plants with medicinal properties is remarkable. Around 70,000 plant species, ranging from lichens to towering trees, are thought to have been employed for medical purposes at some point. Medicinal plants serve as a starting point for the isolation or synthesis of traditional medications.

According to the World Health Organisation (WHO), a medicinal plant is any plant that has compounds in one or more of its organs that have medical value or that serve as building blocks for chemical or pharmacological semi-synthesis. The existence of many complex chemical molecules with varying compositions, known as plant metabolites, particularly secondary compounds, in one or more plant sections is what gives medicinal plants their curative abilities. Primary and secondary metabolites are two types of plant metabolites. In India, using various portions of various medicinal plants to treat particular illnesses has long been popular. In India, the traditional medical systems of Ayurveda, Siddha, and Unani have long been practised. The majority of our knowledge of medicinal plants comes from traditional inheritance.

Traditional medicine is the synthesis of therapeutic experience of generations of practicing physicians of indigenous systems of medicine. Traditional preparation comprises medicinal plants, minerals and organic matters etc. Herbal drug constitutes only those traditional medicines that primarily use medicinal plant preparations for therapy. The ancient record is evidencing their use by Indian, Chinese, Egyptian, Greek, Roman and Syrian dates back to about 5000 years. About 500 plants with medicinal use are mentioned in ancient texts and around 800 plants have been used in indigenous systems of medicine. Indian subcontinent is a vast repository of medicinal plants that are used in traditional medical treatments [1], which also forms a rich source of knowledge. The various indigenous systems such as Siddha, Ayurveda, Unani and Allopathy use several plant species to treat different ailments [2]. In India around 20,000 medicinal plant species have been recorded

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recently, but more than 500 traditional communities use about 800 plant species for curing different diseases [3]. Currently 80 % of the world population depends on plant-derived medicine for the first line of primary health care for human alleviation because it has no side effects. Plants are important sources of medicines and presently about 25% of pharmaceutical prescriptions in the United States contain at least one plant-derived ingredient. In the last century, roughly 121 pharmaceutical products were formulated based on the traditional knowledge obtained from various sources.

*Andrographis paniculata*, a popular medicinal herb, is abundantly available in China, India, and other Asian countries [1,2]. This species' extracts have a variety of biological properties, including hepatoprotective [3,4], antibacterial [5,6], antiinflammatory [5,7], antidiabetic [7,8], and anticancer [8,9]. Deoxyandrographolide and andrographolide are examples of labdane diterpenoids and are the plant's main active components.

## II. PLANT PROFILE OF ANDROGRAPHIS PANICULATA

Mostly found in Tropical Asia, the genus *Andrographis* comprises 28 species of tiny annual herbs. Only a few species have therapeutic value; the most well-known is *Andrographis paniculata* (Burm. f.) Nees, which is part of the Acanthaceae family. It is widely distributed throughout south-east Asia, including Pakistan, Indonesia, India, and Sri Lanka [10,11]. This herbaceous annual is commonly grown in Southern Asia, India, China, and certain regions of Europe. It can be found in the wild in Telangana, Andhra Pradesh, Tamil Nadu, Karnataka, Maharashtra, Orissa, Uttar Pradesh, and Uttarakhand. It grows in a wide range of vegetated areas, including roadsides, villages, pine, evergreen, and deciduous forests. It is simple to grow from seeds in any type of soil. The plant is gregarious and can be found in high numbers in wet, shaded waste areas, as well as in dry forests on occasion. Ayurvedic 'Kalmegh' *A. paniculata* is an erect annual herb with a bitter flavor in all parts of the plant. In north-eastern India, the plant is known as Maha-tita, which translates as "King of Bitters". [12].

### Geographical Distribution:

*Andrographis paniculata* (Burm. f.) Wall. ex Nees is indigenous to Taiwan, China, and India. It can also be found in tropical and subtropical Asia, Southeast Asia, and a few more nations such as Cambodia, the Caribbean islands, Indonesia, Laos, Malaysia, Myanmar, Sri Lanka, Thailand, and Vietnam. This plant can also be found in various phytogeographical and edaphic zones in China, America, the West Indies, [11] It can be found in the wild across India's plains, particularly in Andhra Pradesh, Tamil Nadu, Karnataka, Maharashtra, Orissa, Uttar Pradesh, and Uttarakhand. [12]

### Description of the plant:

Grows In moist, shady conditions, the plant grows upright to a height of 30-110 cm (12-43 in). The slender stem is dark green in color, square in cross section, and has longitudinal furrows and wings along the angles. The glabrous blades of the lance-like leaves measure up to 8 cm (3.1 in) long by 2.5 cm (0.98 in) wide. The fruit is a 2 cm (0.79 in) long and a few millimeters diameter capsule. It has numerous yellow-brown seeds. [13, 14]

Synonyms: *A. paniculata* var. *glandulosa* Trimen., *Justicia paniculata* Burm. f

Common Names: king of bitter" or green Chiretta in English. Kalmegh" in Hindi, "Chanxinlian" in Chinese, "fah tha lai" in Thai, and "Hempedubumi" in Malaysian

### Taxonomical Classification:

Kingdom: Plantae

Division: Angiosperms

Class: Eudicots

Clade: Asterids

Order: Lamiales

Family: Acanthaceae

Genus: *Andrographis*

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

Biological name: *Andrographis paniculata*



Fig 1: *Andrographis paniculata*

**Vernacular Names [13]:**

Language	: Local name	Language	: Local name
Telugu	: Nilavembu	Chinese	: Chuan Xin Lian
Sanskrit	: Kalmegha, Bhunimba	Burmese	: Se-ga-gyi
Hindi	: Kirayat, Kalpanath,	French	: Chiretteverte, Roidesamers
Tamil	: Nilavembu	Indonesian	: Sambiroto, Sambiloto
Kannada	: Nelaberu	Japanese	: Senshinren
Malayalam	: Nelavepu, Kiriyaattu	Konkani	: Vhadlem Kiratyem
Marathi	: Oli-kiryata, Kalpa	Lao	: La-Sa- Bee
Bengali	: Kalmegh	Malay	: HempeduBumi, Sambiloto
Gujarati	: Kariyatu	Russian	: Andrografis
Panjabi	: Chooraita	Persian	: Nain-eHavandi
Oriya	: Bhuinimba	Philippines	: Aluy, LekhaandSinta
Manipuri	: Vubati	Scandinavian	: GreenChiratta
English	: TheCreat, KingofBitters	Sinhalese	: HinKohombaorHeenKohomba

**Ethano Medicinal Uses:**

It has been widely used for the treatment of sore throat, flu and upper respiratory tract infections, treat bacterial dysentery, carbuncles, colitis, tuberculosis, malaria, herpes, ulcer and venomous snake bites, used to treat fever, the common cold and diabetes.

**Ayurvedic Uses:** According to Ayurvedic literature, the plant has Kasaya rasa, Ruksha guna, Shita virya, and Katu vipaka. Krinnroga (worm infection), gandamala (scrofula), apaci (cervical lymphadenitis), and vrna are all treated with the stem bark of *B. variegata* (wounds).

**III. PHYTOCHEMICALS REPORTED**

Andrographolide, 14-deoxy-11,12-didehydroandrographolide (14DDA) and neoandro-grapholide (Fig.2) are examples of the major labdane diterpenoids isolated from *A. Paniculata*. The extract of the plant and its major compounds were having a broad range of pharmacological properties, including hepatoprotective, hypoglycemic, cardioprotective, anti-inflammatory, immunostimulatory and anticancer activities.

The plant *Andrographis paniculata* is a rich source of some bio active molecules such as labdane type terpenoids, Steroids, Flavanoids, Glycosides etc. Some of the reported phytochemicals are listed below in the (table1) and (Fig3to 6)

Author	Title of the work	Plant part used	Isolated compounds	Journal
Matsuda T et al., 1994 [15]	Cell differentiation-inducing diterpenes from <i>Andrographis paniculata</i> Nees	aerial part	14-epi-andrographolide, iso-andrographolide, 14-deoxy-12-methoxyandrographolide, 12-epi-14-deoxy-12-methoxyandrographolide, 14-deoxy-12-hydroxyandrographolide, 14-deoxy-11-hydroxyandrographolide, 14-deoxy-11,12-didehydroandrographolide, 6'-acetylneoandrographolide, bis-andrographolides A, B, C and D,	ChemPharmBull (Tokyo) 1994; 42:1216-1225
Dua et al. 2004 [16]	Anti-malarial activity of some xanthenes isolated from the roots of <i>Andrographis paniculata</i>	Roots	1,8-dihydroxy-3,7-dimethoxy xanthone, 4,8-dihydroxy-2, 7-dimethoxyxanthenes, 1,2-dihydroxy-6,8-dimethoxyxanthone and 3,7,8-trimethoxy-1-hydroxyxanthone.	J. Ethnopharmacol, 2004;95:247-25.
Y. Koteswara Rao et al., 2004 [17]	Flavonoids and Andrographolides From <i>Andrographis paniculata</i>	whole plant	5,7,20,30-tetramethoxyflavanone and 5-hydroxy-7,20,30-trimethoxyflavone, as well as several other flavonoids, andrographolide diterpenoids, and polyphenols	Phytochemistry 2004;65:2317-2321
Kai-Lan Zhou et. al, 2008 [18]	Two new ent-labdane diterpenoid glycosides from the aerial parts of <i>Andrographis Paniculata</i>	aerial parts	3-O-b-D-glucosyl-14-deoxyandrographiside and 3-O-b-D-glucosyl-14-deoxy-11,12-didehydroandrographiside	Journal of Asian Natural Products Research, Vol. 10, No. 10, October 2008, 939-943.
Maria Carmen S. et al, 2016 [19]	Secondary Metabolites from <i>Andrographis paniculata</i> (Burm.f.) Nees.	aerial parts	squalene, polyprenol, lutein, chlorophyll a, and a mixture of $\beta$ -sitosterol, stigmasterol, $\alpha$ -amyrin acetate, triacylglycerols	Der Pharmacia Lettre, 2016, 8 (13):157-160.

**Table1:** Reported phytochemicals from *A. paniculata*

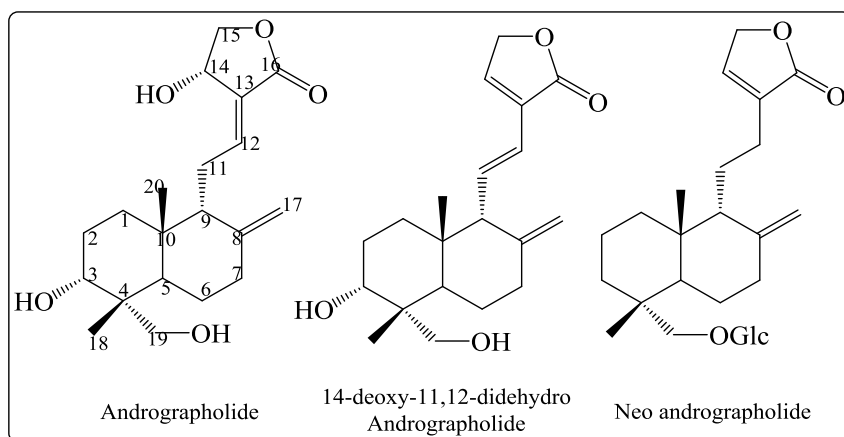


Figure2: Structures of major bioactive compounds from *A. paniculata*

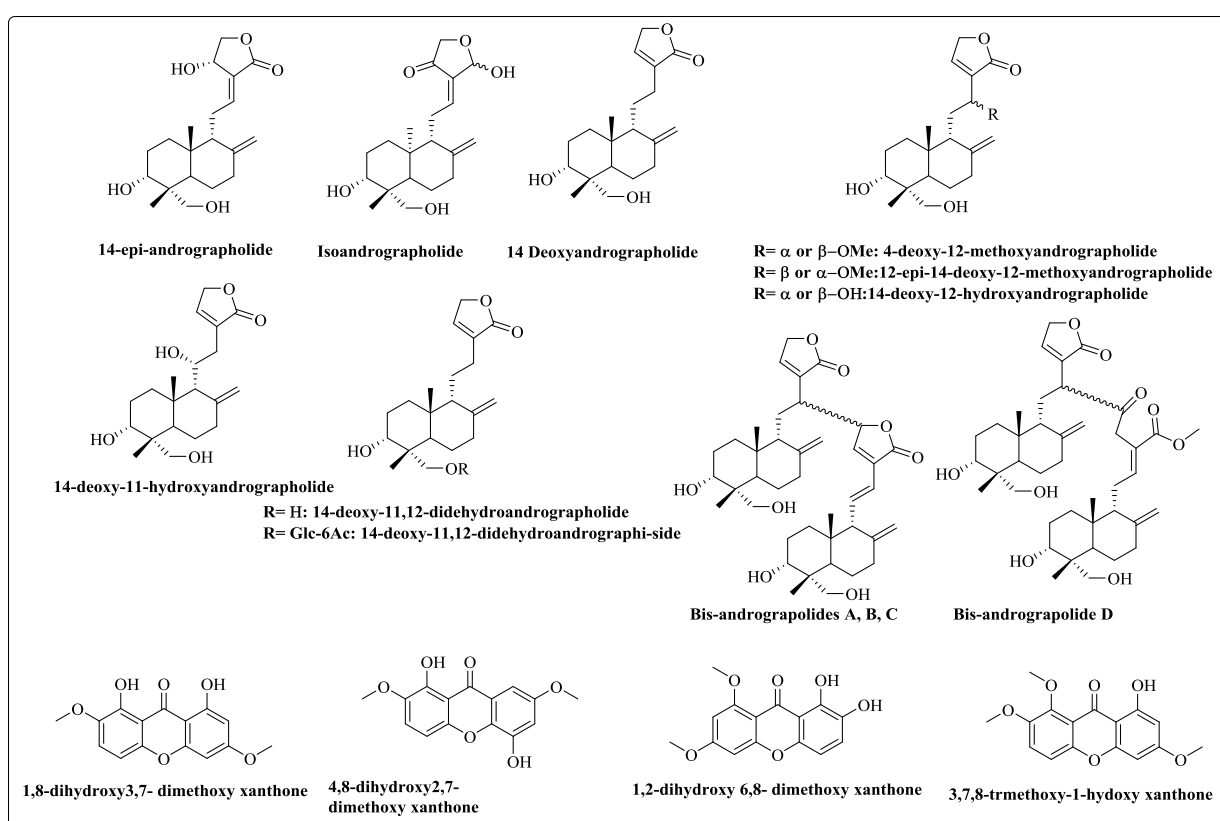


Figure3: Structures of reported phytochemicals from *A. paniculata*.

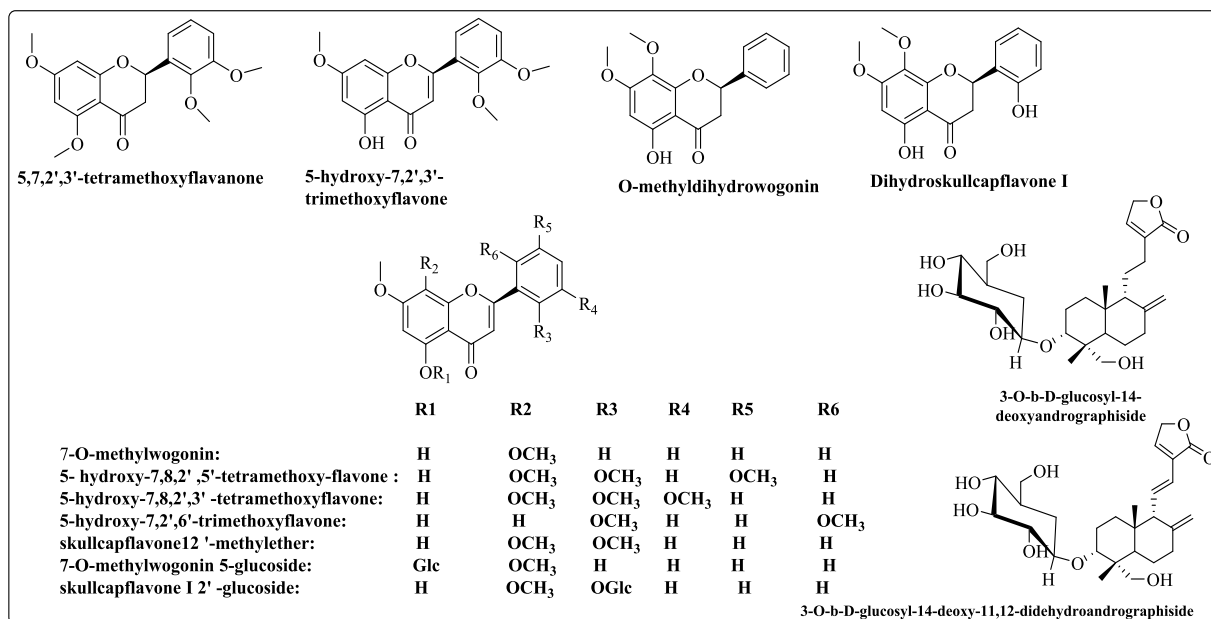


Figure4: Structures of reported phytochemicals from *A. paniculata* 1.

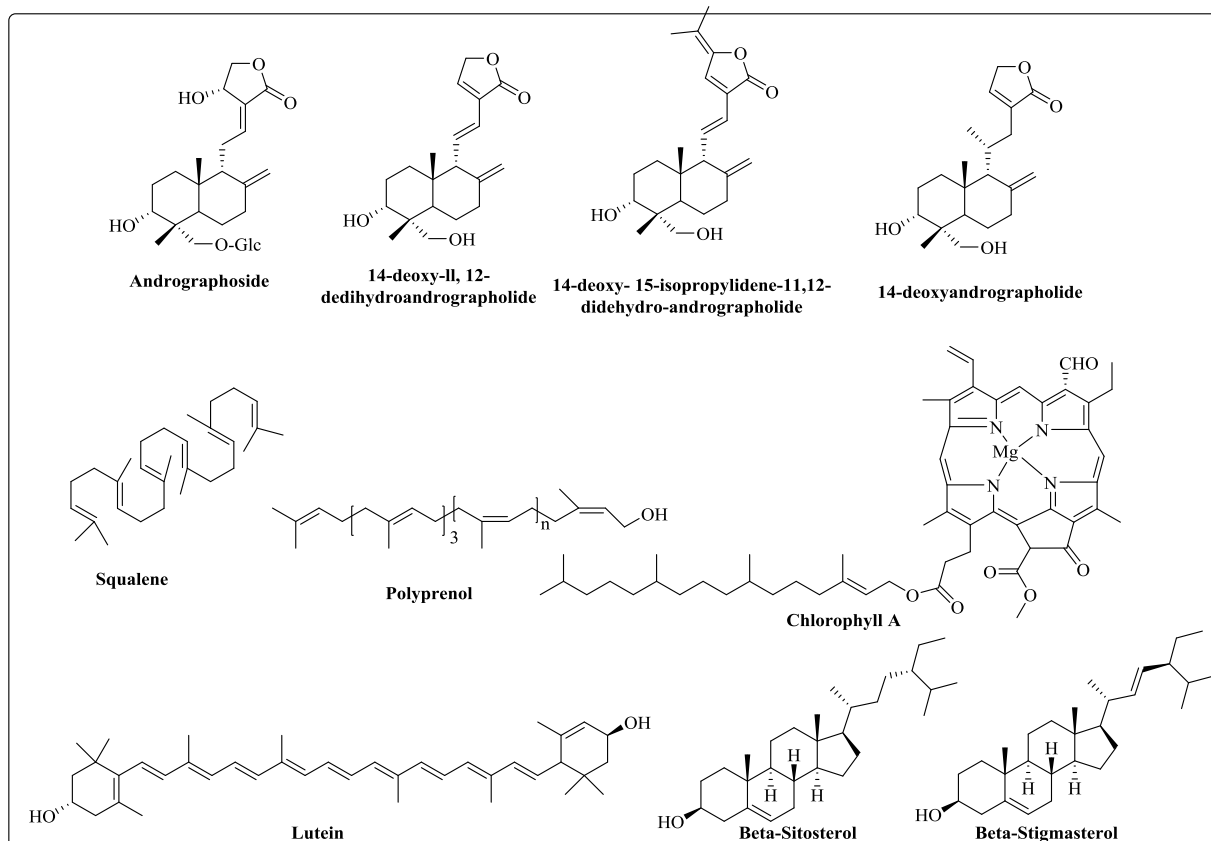
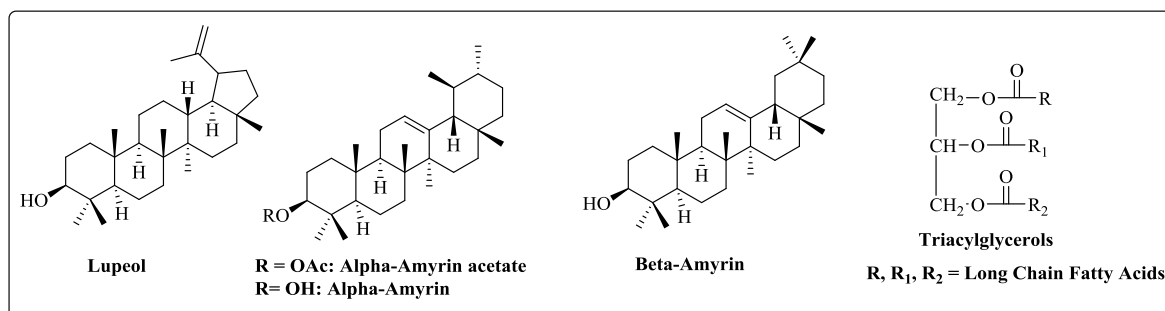


Figure 5: Structures of reported phytochemicals from *A. paniculata* 2



**Figure6:** Structures of reported phytochemicals from *A. paniculata* 3.

#### IV. REPORTED PHARMACOLOGICAL ACTIVITIES

The plant *A. paniculata* has large range of bioactivity profile. Reported activity studies are listed below in the table.

Author	Title of work	Reported activity	Method	Reported journal
SimicMG [20]	Mechanisms of inhibition of free-radical processes in mutagenesis and carcinogenesis	Antioxidant	The mechanisms of the defence system against genotoxic damage are discussed, with an emphasis on free-radical activities. The components of the defence system, their interrelationships, and the stages of defence are all described.	Mutation Research. 1988;202(2): 377-386
Puri A et.al, [21]	Immunostimulant agents from <i>Andrographis paniculata</i>	Immunomodulatory Activity	In mice, EtOH extract and isolated diterpene andrographolides from <i>Andrographis paniculata</i> (Acanthaceae) stimulated antibody and delayed type hypersensitivity (DTH) responses to sheep red blood cells (SRBC).	Journal of Natural Products. 1993;56(7):9 95-999.
Madav S et.al, [22]	Analgesic, antipyretic and antiulcerogenic effects of andrographolide.	Antipyretic and Analgesic	At a dose of 300 mg/kg, it demonstrated considerable (P<0.05) analgesic effect in the Randall Selitto test in rats and acetic acid-induced writhing in mice. In rats with Brewer's yeast-induced pyrexia, andrographolide (100 and 300 mg/kg, oral) had a substantial (P < 0.05) antipyretic effect three hours after administration.	Indian Journal of Pharmaceutical Sciences. 1995;57(3):1 21-125
Dua VK et.al, [23]	Antimalarial activity of different fractions isolated from the leaves of <i>Andrographis paniculata</i> .	Antimalarial	Studies showed that Both the n-hexane extract and the isolated chemicals' suppression of heme polymerization activity are categorised as good and may have antimalarial properties.	Journal of Medicinal and Aromatic Plant Sciences. 1999;21:106 9-1073.
Trivedi NP et.al, [24]	Hepatoprotective and antioxidant property of <i>Andrographis paniculata</i> (Nees) in BHC induced liver damage in mice.	Hepatoprotective	The administration of AP demonstrated protective effects on glutathione levels and the activities of glutathione reductase, superoxide dismutase, catalase, and glutathione peroxidase. Lipid peroxidase's activity was similarly lowered.	Indian Journal of Experimental Biology. 2001;39(1):41 -46.
Batkhuu.Jet.al, [25]	Suppression of NO production in activated macrophages in vitro and ex vivo by neoandrographolide isolated from <i>Andrographis paniculata</i> .	Anti-Inflammatory Effects	<i>Andrographis paniculata</i> has been shown to have suppressive effects both in vitro and in vivo on the production of nitric oxide (NO) in mice peritoneal macrophages that have been activated by lipopolysaccharide (LPS) and provoked by bacillus Calmette-Guérin (BCG).	Biological & Pharmaceutical Bulletin. 2002;25(9):11 69-1174.
Rajagopal S et.al, [26]	Andrographolide, a potential cancer therapeutic agent isolated from <i>Andrographis paniculata</i> .	Anticancer	This study identifies the cellular targets and processes that are affected by andrographolide therapy in immune cells and human cancer cells. The in vitro growth of several tumour cell lines, which represent distinct cancer types, was suppressed by andrographolide therapy.	Journal of Experimental Therapeutics and Oncology. 2003;3(3):1 47-
Kumar K et.al, [27]	Antiviral properties of ent-labdene diterpenes of <i>Andrographispani</i>	Antiviral Effects	Among the diterpenes identified from <i>Andrographis paniculata</i> , neoandrographolide, 14-deoxy-11,12-didehydroandrographolide, and ent-	Phytotherapy Research. 2005;19(12): 1069-1070.

	<i>culata</i> Nees, inhibitors of herpes simplex virus type 1.		labdene exhibited viricidal efficacy against herpes simplex virus 1 (HSV-1).	
Borhanuddin M et.al, [28]	Hypoglycaemic effects of <i>Andrographis paniculata</i> Nees on non-diabetic rabbits.	Antihyperglycemic	Its hypoglycemic impact has been tested in a variety of ways. Water extract of AP 10 mg/kg body weight significantly (P 0.001) prevents hyperglycemia induction induced by oral administration of glucose 2 mg/kg body weight.	Bangladesh Medical Research Council Bulletin. 1994;20(1):24–26.
Singha et.al, [29]	Antimicrobial activity of <i>Andrographis paniculata</i> .	Antimicrobial	The antibacterial activity of <i>Andrographis paniculata</i> aqueous extract, andrographolides, and arabinogalactan proteins was investigated. The combined action of the separated arabinogalactan proteins and andrographolides resulted in substantial antibacterial activity in the aqueous extract.	Fitoterapia. 2003;74(7-8):692–694
Arunotayanun, et.al, [30]	A Comprehensive Review of <i>Andrographis paniculata</i> (Burm. f.) Nees and Its Constituents as Potential Lead Compounds for COVID-19 Drug Discovery	COVID-19 Drug Discovery.	According to in silico and in vitro investigations, the active compounds in <i>A. paniculata</i> have potential actions against 3CLpro and its virus-specific target protein, human hACE2 protein; they also suppress infectious virion generation.	Molecules 2022, 27, 4479. https://doi.org/10.3390/molecules27144479h

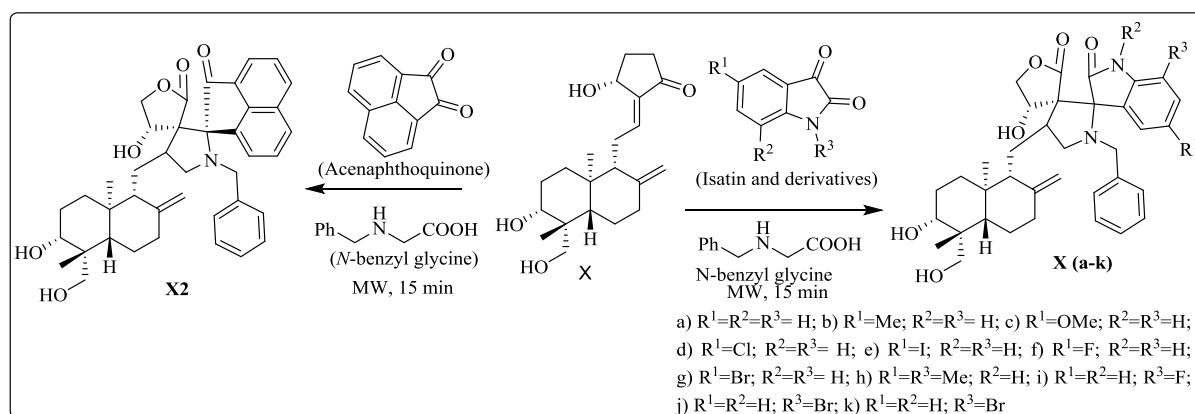
**Table2:** Reported activity studies on *A. paniculata*

## V. REPORTED CHEMICAL TRANSFORMATIONS ON ANDROGRAPHOLIDE

Extensive libraries of andrographolide analogues have been synthesized mainly by modifying the  $\alpha,\beta$ -unsaturated  $\gamma$ -butyrolactone moiety, the two double bonds  $\Delta^8$ , [31] and  $\Delta^{12}$ , [32] and the three hydroxyls at C-3 (secondary), C-14 (allylic) and C-19 (primary). Many of these synthetic analogues exhibit superior anticancer activity over the naturally occurring andrographolides.

### Di-Spiro andrographolide derivatives

D. Chakraborty *et al.* have been synthesized Di-spiro andrographolide derivatives from andrographolide **X**, when it was reacted with substituted isatins/acenaphthoquinone and *N*-benzyl glycine via azomethine ylide cycloaddition reaction, yielded a library of dispiro analogues **Xa-k**, **X2** containing both spiro-oxindole and pyrrolidine/pyrrolizidine rings attached to andrographolide (Fig-7). Cytotoxic effect of the all synthesized derivatives has been studied against MCF-7 breast cancer cell lines. [33]



**Figure 7:** Synthesis of Di-Spiro andrographolide derivatives

### $\beta$ -amino- $\gamma$ -butyrolactone analogues

S. Kasemsuk *et al.* have been synthesized a series of  $\beta$ -amino- $\gamma$ -butyrolactone analogues from naturally occurring andrographolide via one pot tandem aza-conjugate addition–elimination reaction (Scheme x) By using economic procedure without any base or catalyst at room temperature, the products 4a-o obtained were in fair to

excellent yields with high stereo selectivity (Fig-8). The cytotoxicity of all new amino analogues were evaluated against six cancer cell lines and revealed their potential for being developed as promising anticancer agents.[34]

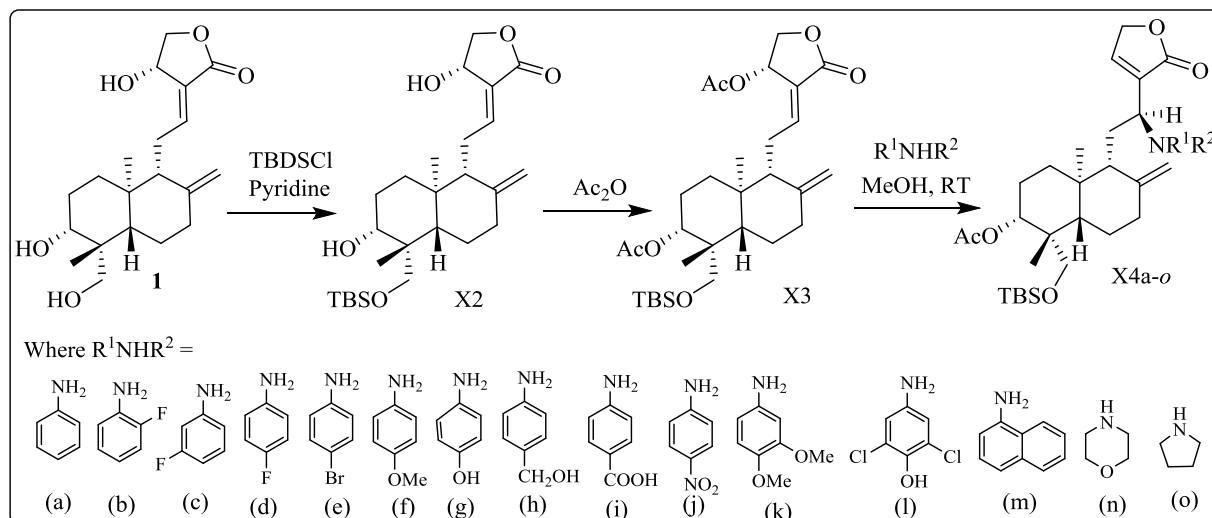


Figure 8: Synthesis of  $\beta$ -amino- $\gamma$ -butyrolactone analogues of andrographolide

### 3,19-O-esters/ether derivatives

S. Wei *et al.* have been synthesized two series of andrographolide **1**, via esterification and etherification of 14-dehydroxy-11,12-didehydroandrographolide. 14-dehydroxy-11,12-didehydroandrographolide **2** was prepared from **1** in high yield using Pyridine/ $Al_2O_3$  under reflux conditions. Compounds **3a-k** were obtained by esterification of the two hydroxyl groups at C-3 and C-19 with either aromatic or aliphatic acids, both mono- and di-esters were prepared. Compounds **4a-f** were prepared via acid-catalyzed etherification of **2** with appropriate aromatic aldehydes (Fig-9). Structurally diverse groups and hetero-atoms were incorporated (Phenyl rings with electron-withdrawing or electron-donating substituents, as well as a furan ring into the side chains and investigated their effects on cytotoxicity [35].

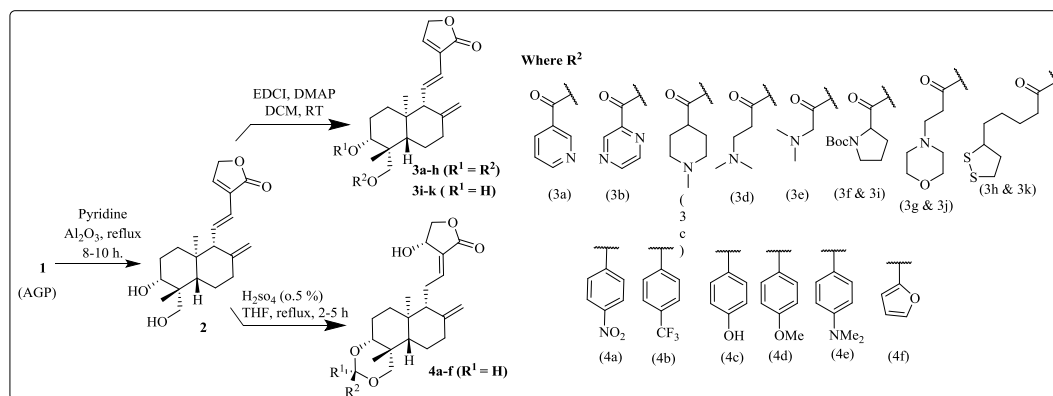


Figure 9: Synthesis of 3,19-O-esters/ether derivatives of andrographolide

### 14-O-acetates Andrographolide

Zhi-Gang Chen *et al.* have been synthesized a series of andrographolide derivatives **xa-f** with excellent regioselectivity and high yield by means of immobilized lipase Novozym 435 –catalyzed enzymatic acylation in acetone. [36] The acylated andrographolide derivatives were tested for antibacterial activity (Fig-10).



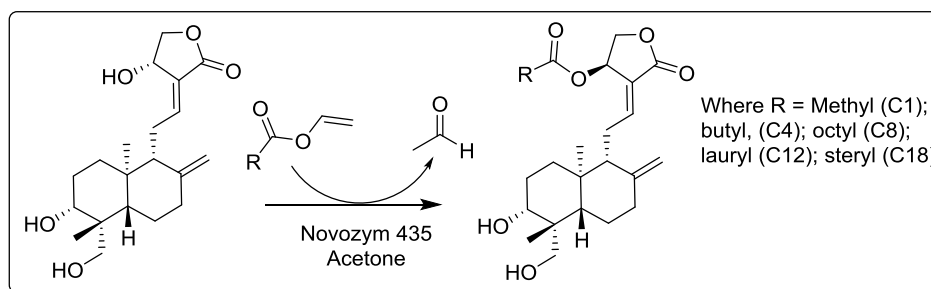


Figure10: Synthesis of 14-O-acetates of andrographolide

### Andrographolide-14-O-Esters

Zhongli Wang, Pei Yu et al. have been synthesized a series of andrographolide derivatives through a facile condensation reaction with different carboxylic acids.[37] The compounds also screened for antibacterial activity. (Fig-11).

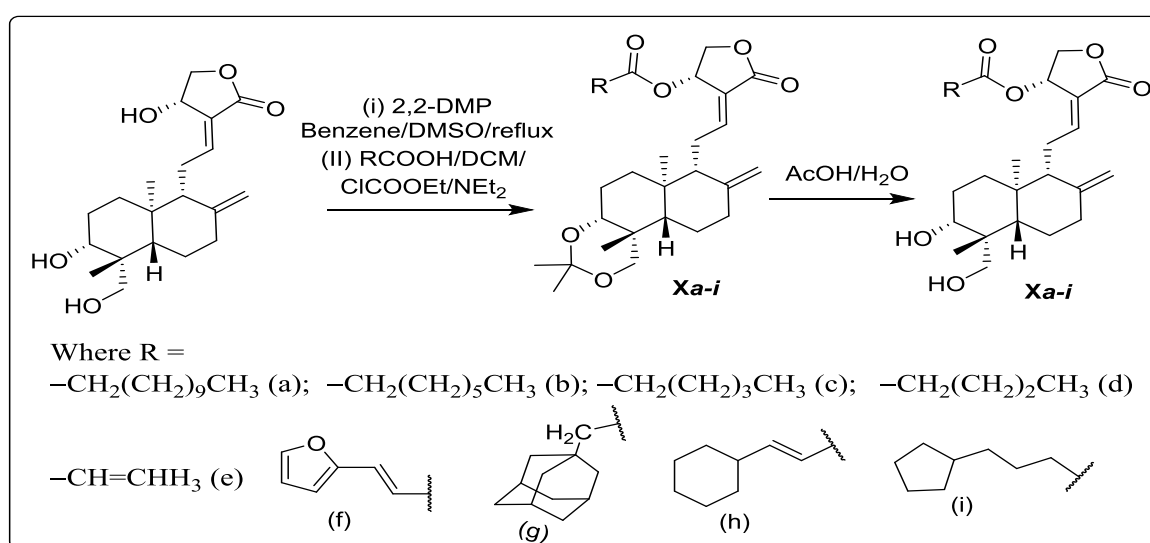


Figure 11 Synthesis of andrographolide-14-O-esters

## VI. CONCLUSION

The aim of this evaluation was to compile the research conducted so far by several researchers in different places in order to establish a preliminary basis for future studies.

The information that is now available on *Andrographis paniculata* also amply illustrates the plant's wide range of pharmacological characteristics. The *Andrographis paniculata* can be considered as a remedy because it has a wide range of pharmacological actions. However, a clinical investigation is required to validate the pharmacological properties of AP that have been examined.

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