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Reviewarticle

Andrographispaniculata(Burm.f.)Wall.exNees.-Apotentherbwith immense pharmacological potential

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ABSTRACT

Medicinalplants,asautochthonoussourcesofmedications,havebeenutilizedsinceprimevaltimes.Andrographis paniculata (AP) is considered one of the most potent herbs around the world. Otherwise known as Kalmegh, the herbhastraditionallybeenusedasacureforthecommoncold,diarrhoea,jaundice,andfeverowingtonumerous causes.Apartfromthis,theherbalpartscanactasliverintoxicantsaswellascardiovascular(CVD)vigorandare also considered to possess free radical scavenging activity. Habitation, season, and harvesting time of the crop have an effect on phytochemical composition that extensively differ from one part to another. In this review, we discussedtheethnobotanyofthisplantbriefly.Apartfromthesevariouspharmacologicalactivitieswithaspecific focus on anticancer properties of the herb are also proposed.

***Keywords*:** *Andrographis paniculata* (AP), andrographolide, anticancer, ethnopharmacology, pharmacological potential.

INTRODUCTION

Andrographis paniculata (Burm.f.) Wall. ex Nees., belongs to the Acanthaceae Family- is an annualherbaceousplantandisgenerallycultivated inSouthernAsia,China,andpartsofEurope.The herbisusuallyrenownedaskalmegh,bhumineeb, and chirayata. It is a valued traditional medicinal plantandhasitsusageintheUnaniandAyurvedic medicinesystems(Chopra *etal*.,1956).Theherb iscommonlyusedtonormalizebodyheat,dissipate toxic materials from the body; preclude common cold,infectionsoftheupperrespiratorytractaswell as sinusitis and fever (Gabrielian *et al*., 2002). It alsoactsasanantidoteagainstsnakesandinsects' venom (Samy *et al*., 2008).Phytochemical screeningofvariousorganicsolventextractsofAP plant parts, such as leaves and bark of the stem exhibitedtheavailabilityofglycosides,phytosterol, saponins, tannins, flavonoids, and terpenoids. Terpenoids are considered to be the crucial constituents in the leaves as well as stem barks (Pandey *et al*., 2019). The occurrence of vital phytochemicalsinAPmakestheplantvaluablefor treating altered ailments and has the potential of providing useful drugs for human use (Pandey *et al*., 2019). This paper will provide a deep insight intotheethnobotany,afewagronomictechniques, adepictionofthepotentchemicalcomponents,and the pharmacokinetics of Kalmegh. Furthermore, chemical possessions, biological roles, and their probablemodesofactionarealsotobeconsidered. The plant has been reported to unveil several meansofbiologicalactivities*invivo*aswellas*in vitro*suchas,anticancer(Iruretagoyena*etal*.,2005; Li *etal*.,2007),anti-inflammatory(Wen *etal*., 2010),immunomodulating/immunostimulatory (Calabrese*etal*.,2000),antihyperglycemic, antihyperlipidemic, hepatoprotective, cardiovascular,antiviral(Wiart*etal*.,2005), antimalarialandfilaricidal,antidiarrheal, antibacterial (Singha *et al*., 2003; Mishra *et al*., 2009).Thedistinctivesecondarymetabolitesencoun teredinthisherbhavesubstantiallyenriched its eminence in the arena of medicinal herbs. The quantitativedeterminationofpharmacognostic parameterswillfacilitateinsettingstandardsfor crudedrugs(Sharma*etal*.,2012).

Vernacularnames

The herb is famous in diverse local languages inseveral parts of the world. In Hindi, the herb is famousas Kalmegh,Kiryat,andMahatit.Theherb iswellknownasKiriyataandOlikiriyatinGujrati. In Malyalam, it is called asNilaveppu, Kiriyatta. WhereasNelaVemuandNilavempuiarethecommon namesinTeluguandTamilrespectively. Bhuinimb,Kirata,andMahateetarethelocalnames in Sanskrit. English: Creat, Green Chirayta, King of bitters (Verma *et al*., 2019).

Origin

KalmeghisaninhabitantofTaiwan,India,and Chinese province. The herb is usually located in Asia's tropical and warm temperate evergreen forests. The mainland of Southeast Asia (the Caribbean islands, Indonesia, Malaysia) and Sri Lanka,aretheothercontinents,wheretheherbcan beeasilyfound.Thisplantisalsofoundinaltered geographical conditions of America, the West Indies,andChristmasIsland(Verma*etal*.,2019).

Geographicaldistribution

Thespecies is native to tropical South-EastAsia and have its presence throughout warmer parts of India. The species is scattered in tropical Asian realms, frequently in remote areas. The herb can be sited in an array of habitations, for instance, plains, hillsides, coastlines, and disturbed and cultivatedareas(roadsidesandfarms)(Niranjan*et al*.,2010;Mishra*etal*.,2007).Nativepopulations ofAPextendthroughoutsouthIndiaandSriLanka which conceivably exemplify the epicenter of origin and diversity among species. The herb is an introduced speciesin northern parts of India, Java, Malaysia, Indonesia, the West Indies, and elsewhereintheAmericas.Thespeciesalsooccurs in the Philippines, Hong Kong,Thailand, Brunei, Singapore,andotherpartsofAsia,whereitmayor may not be native (Perumal Samy *et al*., 2017). Contrastingotherspeciesof the genus, *A. paniculata*isofprevalentoccurrenceinmostplaces inIndia,togetherwiththeplainsandhillyareasup to an elevation of 500m (1,600ft). In India, the principalsourceofplantsiscollectedfromitswild habitat.AccordingtotheIUCNdatabase,theplant is regarded as Low Risk or of Least Concern (Gowthami *et al*., 2021).

Climateandsoil

The herb is a hardy species in tropical and subtropical regions and therefore thrives well in almost all types of soil. However, soils relatively superior in heavy metals such as Al, Cu, and Zn are preferred for the crop. Medium productive sandyloamtoclay-loamsoilswithapHrangeof 6.5 -8.5 is ideal for the cultivation of the crop. Though it is cultivated in open fields still can withstandpartialshadeoftrees(Verma*etal*.,2019).

Propagationandnurseryaspect

Both seed and vegetative methods can be utilizedforraisingtheherb.However,propagation through seed is easy and economical when the cultivationisofcommercialimportance.Towards thebeginningofSeptemberseedsoftheherbhave beensowninnurserybeds,aftersoakinginwater. About650-750gofseedsistherequisiteforraising a nursery for one hectare of land (Verma *et al*., 2019). Seeds are usually sown in nursery beds preparedbytakingamixtureofnormalsoil,sand, and organic matter in a ratio of 1:1:1 and at a spacingof5cminrows.Ittakesaround8-10days forgerminationtocommence.Thedirectsowncrop isscatteredthinlywithaseedproportionof1.5kg per hectare (Verma *et al*., 2019).

Agronomictechniques

Plants of Kalmegh traditionally grow through seedculture.Therecommendedtimeforsowingis usually from May to July. However, seed latency isaforemostlimitationinthecommercialfarming ofAP.Applicationofphytohormonesandtreatment with hot water has been recommended, to prevail over this problem (Kumar *et al*., 2011). The technique is not adequate as per the commercial measuresconcernedduetoinconsistencyamongst thesciondsderivedfromseedsandthedeferredroot systemofseedlings(Martin*etal*.,2004).Numerous non-traditional proliferation approaches, for instance,micropropagationtechniquesaretherefore the alternatives to generate huge amounts of saplingsinasmallduration,aswellastoimprove phytochemical contents in AP (Vijaylaxmi and Murthy,2012).Theyieldoftheherbisinfluenced byplantingandtimeofharvesting(Nemade*etal*., 2003).

Landpreparationandfertilizerapplication

Thelandshouldbeorganizedwellbyfrequent ploughing to make the soil pounded. Organic manure at a rate of 20 t $ha^{-1}$is applied as a basal application. An NPK fertilizer at a proportion of 75:75:50kgha^{-1}shouldbegivenintwosplitdoses. Thefirstdoseisattheplantingstage,followedby the second; that is 40 days after plantation. The employof Azospirillium(5 kg) along with Phosphobacteria (5 kg) ha^{-1} will give satisfactory results.

Transplantingandoptimumspacing

The nursery-raised seedlings are transplanted inthemainfield,uponreaching10-25cmwithan optimumdistanceof30x30cmfromplanttoplant and row to row (Ram *et al.*, 2008; Kanjilal *et al.*, 2002).

Irrigationandweeding

Light irrigation as per prerequisite can be provided at regular intervals to aid the early establishment of seedlings, once the transplantation has been done. There is no need for additional irrigationasthecropistransplantedintheseason of monsoon.Whenever there is a requirement for water,thefieldcanbeirrigatedatintervalsof20- 25 days (Verma *et al*., 2019).

Kalmeghis a short-durationcrop and is cultivatedinthe*Kharif*season.Thus,weedinvasion is an immense issue that deteriorates the quality and quantity of herbs. Since it is an herbaceous plant,thefieldshouldbefreefromweeds.Twoto three weddings, usually one after 20 days and another after 60 days of plantation are essential during the crop season. The appliance of the herbicidependimethalinattherateof1kgha^{-1}as pre-emergencefollowedbyquizalofopethylatthe rate of 50 g per hectare as post-emergence was found to be an efficient weed control agent. This shouldbefollowedbyonemechanicalweedingfor accomplishing high biomass yield (Meena *et al.*, 2017; Semwal *et al*, 2016). There were no major insectpestsordiseaseinfestationhasbeenrecorded inKalmegh.BrownScale, *Parasaisettianigra*,was found to causing considerable damage, with the affectedplantsshowingstuntedgrowthanddrying. Semilooper,*Panillaalbopenstata*dentedtheplants byfeedingonyoungleaves,flowerbuds,andtender pods (Rani and Sridhar, 2005). Application of Azadirachtin(1-2%)leafextractuponthe herbwas foundtobehelpful(SuganthyandSakthivel,2013).

Cropmaturityandharvesting

Generally, the crop matures after 120 days of sowing in October and November. Most pods mature fully in January and February (Verma *et al*., 2019). The planting and harvesting period influences the yield and quality of the crop. The active principle of the plant varies with time intervals and diverse environmental conditions (Kumar *et al*., 2002). It is harvested when most plants are in bloom. Upon maturity, the plants should be uprooted leaving few healthy plants in the field for seed production. The fruits once mature, should be picked up and dried in the sun for seed collection (Wankhade *et al*., 2005).

Postharvestmanagementandstorage

Afteruprootingtheplant,itshouldbesun-dried fortwodaysfollowedbyshadedrying.Oncedried, thematerialswerepackedingunnybagsandstored in dark, airy, and moisture-free places.The crops harvestedafterthreemonthsofcultivationshowed the utmost sum of andrographolide, a foremost bioactive compound of AP followed by that just beforehandtheflowering period(Tipakorn,2002).

Yieldandcostofcultivation

MostoftheStatesofIndiahavebeenreported for the commercial cultivation of Kalmegh, with an average yield (as a whole plant) of 2.5 t ha^{-1}. The approximate cost of the crop for one hectare comes to around INR 25,000/-.

Trade

Underthetradeappellation Kalmegh,onnormal 2,200-5,500 t of the herbage is traded in India.

Phytochemistry(chemicalconstituents)

Andrographolide (AD) is one of the foremost compound among the active principles that were extracted from the leaves and roots of Kalmegh. The compound is highest in the leaves; where as seedshavethelowestpossiblecontent(Sharma*et al*., 1992). Diterpenoidssuch as deoxy and rographolide-19-ß-D-glucoside and neo-and rographolidearetwoofthebittercomponentsthat have beenisolated fromthe leaves(Weimingand

Xiaotion,1982).Therootswerefoundtoberichin apigenin-7,4'-di-O-methylether,andrographolide, andanovelnaturalflavone,5-hydroxy-7,8,2',3'-tetramethoxyflavone($C_{19}H_{18}O_7$).Andrographlide D (14-deoxy-11, 12-didehydroandrographolide), homoandrographolide,andrographan, andrographon,andrographosterinandstigmasterol are the other components reported in the herb (Siripong*etal*.,1992).Flavonoids,comprising5, 7,2',3'-tetramethoxyflavanone,alongwithother flavonoids, andrographolide diterpenoids, and polyphenols, were acquired from the entire plant (Koteswara Rao *et al*., 2004). The above said phytoconstituentsareconsideredtobeaccountable forvariouspharmacologicalactivitiesoftheherb.

Pharmacologicalpotential(medicinal properties)

AccordingtoAyurvedatheherb"Kalmegh"is astringent, pungent, cooling, laxative, wound healing(vulnerary),antipyretic,antiperiodic,anti-inflammatory, expectorant (Mucoactive agents), depurative,sleep-inducing(soporific), anthelmintic, digestive, and stomachic. The herb is a valuable agent againsthyperdispsia, burning sensation, ulcers, fevers, skin diseases, leprosy, colic, flatulence, diarrhoea,dysentery,and haemorrhoids, etc. (Mall and Tripathi, 2016). Kalmeghis alsorenownedas an apparent Homoeopathic drug. Fresh leaves of the herb are used to prepare "Alui", a well-known household medicine in Bengal (India), and are given to childrensufferingfromstomachcomplaints.Ithas also been proven to be a hepatoprotective drug. Blockingofthevoltage-operatedcalciumchannels aswellasinhibitionofCa(+2)influxbythedried herbal extract induces relaxation of the uterus (Hancke *et al*., 1995). Initial studies in animals ascertainedthatAPmighthelpcurecardiacdisease (Zhao,andFang,1991;Zhang,andTan,1997).It appearstostimulategallbladdercontraction,aswell asprevent blood clots (Varies, 1993).The herb also showedcertainotherphytochemicalpropertiesas described below:

1. Anticancereffect

Andrographolide,the majorbioactive compoundofKalmeghshowedprominenteffects on malignant cells due to hindrances in the proliferationofcells,arrestofthecellcycle,orcell discrepancy.Throughinductionofprogrammedcell death of malignant cells, these compounds also enhancetheimmunesystem.Theanticancerability ofADincoloncancercells(HT-29)wasevaluated by Khan *et al*. (2018) and a reduction in cell viabilitywas observed.In a time and dose dependantmanner,theyobservedreducedviability ofthecells.ThecellcycleintheG2andMphases wassurprisinglyinterruptedbyADatlowerdoses. While the cell cycle at the G0/G1 phase was arrestedatahigheramount.Throughameliorating intracellular freeradicallevelsanddisruptionof mitochondrialmembrane potential, these phytoconstituents caused apoptosis of the cancer cells. AD along with another flavonoid isolated from Kalmegh leaves remarkably reticent U251 (CNS) and M14 (melanoma) human carcinoma cellsand thereby proven the anticancer effect of the herb (Agarwal, 2015).

Diterpenoids along with andrographolide and isoandrographolide isolated from Kalmegh have alsobeenexploredbyChenandColleagues(2009) takinghumanleukaemia(HL-60)cells.Thesetwo compounds were more effective compared to others.Adifferentflavonoid,7,8-dimethoxy-2á-hydroxy-5-O-β-d-glucopyranosyloxyflavone,with adosevalue(IC50)of3.50µMextractedfromthe aerial portions of the herb, revealed persuasive antiproliferative activity against leukaemia cells. An improvement in G0/G1 phase cells and a significant decline in the cell amount at the Synthesis Phase and G2 and M stages were observed against HL-60 cells with the use of andrographolide at a dose of 12 μg/mL.

The effective cytotoxic activity of the herbal extracts has been studied by Geethangili *et al*. (2008)againstseveralhumancancercellssuchas lymphocytic (Jurkat), prostate (PC-3), hepatoma (HepG2), and colon cancer cells. Noticeably inhibitionintheproliferationofHT-29coloncancer cells was observed with the dichloromethane fraction of the extract. Inhibition of human colorectal carcinoma (CRC) Lovo cell growth by andrographolide was also reported by Shi *et al*. (2011). Induction in the expression of inhibitory proteins (p16, p21, and p53) of the cell cycle and arrest of the G1-S phases is considered to be responsibleforthis.TheactivityofcyclinD1along withCdk4andcyclinA1/Cdk2necessaryforthe

transition from the G1 to S phase has been overwhelmedby theseproteins.Growth suppression,CRCcellinvasion,andstimulationof apoptosis have been shown by andrographolide recently.

AD repressed the proliferation of lung cancer cells through a reduction in the level as well as a transformation of the growth factor (Luo *et al*., 2014).Inhibitionofmelanomatumourenlargement andmetastasisthroughapoptosisandarrestofthe melanomacellcycleattheG-1phasehasalsobeen shownbyAD.Inotherways,inhibitionofTLR4/ NF-κBsignalingpathways,followedbyinhibition of mRNAand Bcl-6 and CXCR4protein expression, is thoughtto be the underlying mechanism for this activity (Zhang *et al*., 2014).

2. Antihyperglycemiceffect

Effective antihyperglycemic action has been shownbyAPextractsandandrographolidewitha reduction of blood glucose levels through α-glucosidase and α-amylase inhibition. Besides monitoring blood glucose levels, the compounds in a dose-dependent manner can also effectually prevent the onset of insulitis. Consequently, in NOD mice, diabetes development was suppressed and delayed. By improving glucose exploitation and oxidation, AP has been found to lower blood glucose levels in type 2 diabetic rats. Liver restorationofinsulinsignalingmoleculesandlower serum lipid levels are also responsible for this activity (Augustine *et al*., 2014). Additionally, andrographolidecontrolstheTHelpercellsbalance, which enables it to restrictT-cell insinuation into pancreatic cells and maybe avert β-cell death. Thereby, preventing the expansion of type 1 diabetes. For the antihyperglycemicaction, stimulation of the sugar uptake and peripheral tissues oxidation with an increase in insulin level is also taken into consideration.

In both insulin-deficient diabetics and healthy rats, AP had a diminishing effect on blood sugar levels. In diabetic rats, andrographolide significantlyenhancedβ-cellfunctioning,GLUT4 translocation,andbloodglucoselevels.Therewas an ominous decrease in the fasting blood glucose in humans upon administrationof Kalmegh extracts.Anotherbioactiveconstituent,14-deoxy-11,12-didehydroandrographolide,hasalso demonstrated antihyperglycemic action. Therefore, researchers' main focus will be on finding more antihyperglycemic chemicals in Kalmegh along with other medicinal plants to develop a better diabetic treatment alternative.

3. Anti-hyperlipidemiceffect

The major cause of atherosclerosis, which resultsinheartattackandstroke,ishyperlipidemia. Severalmedicinalplantshavebeenutilized,either alone or in combination, for the treatment of *Diabetes mellitus* (DM) since time immemorial. However,inordertoconfirmthesafetyandefficacy of these medicinal plants further scientific and clinical studiesare needed(Fallah*et al*., 2023). Chen*et al*. (2020) foundthatand rographolide and neo and rographolide from AD have antihyperlipidemic properties. Reports by Yang and Song (2014), mentioned the fruitful efficacyof and rographolideand neo and rographolideonhyperlipidemicmousemodels.In a dose-dependent way, these two substances diminished the cholesterol level, which can be confirmedwithadecreaseintheenzymesaspartate transaminaseandalaninetransaminase.Duetothe various regulation of iNOS as well as eNOS expressionintheaortaofhyperlipidemicrats,lipid andlipoprotein-reducingactionsofthesubstances areliabletoincrease.Itisnecessarytoconcentrate futureresearchontheconcurrentsignalingpathway and molecular mechanism.

4. Cardiovascularеffect

AccordingtoWong*etal*.(2020),*A.paniculata* and andrographolidehave bioactivitiesthat decrease the inflammatory response, oxidative stress,apoptosis,cardiacfibrosis,andendothelial dysfunction. By inhibiting the inductive phase of the inflammatory response, mediated by several signaling molecules such as NF-κB, PI3K/ Akt, MAPK,andSTAT3,thephytoconstituentsreduce the signs of myocardial damage. A possible mechanism for the specific action might be the effectonoxidativestresscausedbyactivatingthe nucleartranscriptionfactor,Nrf-2,anddecreasing the enzymesthatproducefreeradicals. Additionally, the phytoconstituents have blocked profibroticgrowthfactors,whichhasreducedheart fibrosisandenhancedendothelialandfibrinolytic function (Wong *et al*., 2020).

5. Antimalarialandfilaricidalactivity

AntimalarialactionofKalmeghrootxanthones against *Plasmodium falciparum* and *Plasmodium bergheio*nanimalmodels(SwissAlbinomice)have been investigated by Dua *et al*. (2004). After treatingthemicewithadoselevelof30mg/kg,a generous reduction (62%) in parasitaemia was observed.1,2-dihydroxy-6,8-dimethoxyxanthone, with a dose level of IC50 > 32 µg/mL was noncytotoxicagainstmammaliancellsinan*in-vitro* cytotoxicity assay. Filaria, a condition in which there is an obstruction of the lymph channels that will lead to Elephantiasis can be efficiently inhibitedwiththeherbalextracts.Fourofthepotent xanthonessuchas4,8-dihydroxy-2,7-dimethoxy xanthone,1, 8-dihydroxy-3, 7-dimethoxy xanthone,3,7,8-trimethoxy-1-hydroxyxanthone, and1,2-dihydroxy-6,8-dimethoxyxanthonewere reported in the roots of the herb. However, substantial antiplasmodial activity against adult worms of *Brugia malayi* was reported by 1, 2-dihydroxy-6, and 8-dimethoxy-xanthone.Though, clues for the pharmacological targets along with the mechanism of action of this compound on*P. falciparum*are still unclear. However,the regulationofatranscriptionfactorisconsideredto beresponsibleforthisphenomenon.Erythrocytes, upon infected with *P. falciparum*, there was an induction of NF-κB regulated inflammatory pathwaysinhumancerebralendotheliumhasbeen observed.Foreffectiveregulationofmalaria,there is a need for the re-evaluation of probable anti-malarial activity of andrographolide against the blood stage of the plasmodial life cycle.

6. Antidiarrhealeffects

Diarrhea is the second leading cause of death, especiallyamongchildrenunderfiveyearsoldin developingcountries.*S.flexneri,S.aureus,E.coli, S.typhi*,and*C.albicans*aretheforemostcausative agents of diarrhea in humans (Ashrafuzzaman *et al*., 2016). Severalplantextractcomprises pharmacologicallyactivesubstanceswith antidiarrheal properties. AP extracts exhibited substantialeffectsagainst*E. coli* bacterial infections. A substantial effect against *E. coli* bacterial infections has been reported. In a case study,patientswithacutebacterialdiarrhoeawere givena500mgdoseofandrographolideforsix daysonadailybasis.Itwasfoundthatthepatients responded favourably to the treatment with an overall effectivenessof 91.3%. Due to its antibacterial activity, the herbal extract was effectiveinbacterialdysenteryaswellasdiarrhea (Perumal Samy *et al*., 2007).

7. Antibacterialactivity

Deathsdue to microbial infectionswere investigated and reported around 9.2 million in 2013, accounting for 17% of overall mortality (Gupta *et al*., 2019; WHO, 2013). The microbes acquireresistancetonumerousantimicrobialdrugs and this is considered to be the sole cause for the ineffectiveness of the drugs. To fight the health problems related to bacterial infections, there shouldbeanimperiousneedforresearchonother therapeutic agents as an alternative source to existing ones (Brown, 2015; Ncube *et al*., 2007). Due to their immense therapeutic activities, plant basedantibacterialcomponentsarethusasuitable remedy for infectious diseases (Shakeri *et al*., 2018).

Theisolatedphytoconstituentsandrographolide fromAPshowedsignificantantimicrobialactivity. Various organic solvent extracts of AP flowers exhibitedantimicrobialactiontoward*S.agalactiae, S.aureus,*and*E.coli*werereportedbySivananthan (2013).Aninhibitoryeffectandthusantimicrobial activity of Kalmegh extract against the urinary tract pathogens for example *E. coli, P. aeruginosa, K. pneumonia, and S. aureus* has been reported *by* Murugesan *et al*. (2018). However, maximum inhibitory action was reported against *E. coli*.

Discussion

There is mention of *Andrographis paniculata* (AP)possessingpotentphytoconstituentsinaltered traditional systems of medicines. Due to various pharmacologicalactivities,theherbhasbeenused as a remedy for hepatic issues, malaria, common colds, cardiovascular diseases, leprosy, stomach problems, etc. The plant has been used to treat hepatic issues, malaria,commoncolds, cardiovasculardiseases,leprosy,stomachproblems, etc.duetovariouspharmacologicalactivities.The prime component accountable for most of the pharmacologicalactionsof the drugis Andrographolide- a diterpene lactone.

Alongwithother diterpenoids isolated fromAP, andrographolide,andisoandrographolidehavebeen reported for their antiproliferative activities by manyauthorsagainstmammaliancelllines.Potent antiproliferative activity by parts of AP against leukaemiacell lines has been reported.An improvementin cells (G0/G1 phase)and a considerabledeclineincellamountagainstHL-60 cellsweremention edwiththe use of andrographolide.Thedichloromethanefractionof theextractreportedaconsiderableinhibitioninthe proliferationofHT-29coloncancercells.Adirect inhibitoryeffectoncancercellswasemployedby andrographolideanditsanaloguesduetoinduction in the expression of cell cycle inhibitory proteins along with depressing cyclin-dependent kinase (Cdk).Asaresult,theprogressionofthecellcycle has been blocked at various stages. In multiple myeloma cells, an inhibition in cell proliferation, and apoptosis, as well as an enhancement in the caspasecascadeactivationwasperceived.AData doseof5μg/gshowed*invivo*anticanceractivityin B16 melanoma mouse cells through inhibition of the TLR4/NF-κB signaling pathway. Reports regarding *in vitro* anticancer activity byAD have also been available in human myeloma cell (OPM1).

APdecreasesthebloodsugarlevelbyescalating itsutilizationandoxidation.Apartfromthisinsulin signalingmoleculesrestorationintheliverandfall intheserumlipidlevelsindicatethepositiveeffects of the compound (Augustine *et al*., 2014). The bloodsugarlevelloweringabilityduetoinhibition of α-glycosidaseandα-amylaseisanotherwaythat proves the antihyperglycemic effects of the AP extractsandandrographolide.Whereas,Yu*etal*., 2003;reportedthattheincreaseofplasmaglucose in rats has significantlybeen attenuated by Andrographolide. Andrographolideand neoandrographolide-two of the potent phytoconstituents have shown hyperlipidemic activity in animal models (mice) (Yang *et al*., 2014). Therewasasignificantreductionofaspartateand alaninetransaminaselevelsintheplasmacompared with simvastatin. The lipid and lipoprotein-reducingeffectsof the compoundsin hyperlipidemic rats are possible due to various regulationstepsofiNOSandeNOSexpression.The activeconstituentsalongwiththeaqueousextracts ofAP exhibited platelet anti-aggregation activity against *in vitro* mouse models(Thisoda *etal*.,2006). APhasthepotentialtoenhanceNO,cyclicGMP, and SOD activity (Wang *et al*., 2020).

Andrographolideshowedapotentialbeneficial effectagainstH9C2cardiomyocytes.Reportswere there on the effective doses for *Kalmegh* herbal extract with treatment duration of 7-31 days against myocardialinjury.Thus,Kalmeghcan be consideredasanalternativesourceforthetreatment of cardiovasculardiseases.However,the effectiveness of these phytoconstituents from the herb against myocardial injury in humans along with clinical trials is yet to be investigated. The mice upon treatment with the herbal extract of andrographis showed a substantial reduction in parasitaemia.Theringstageoftheparasite,during the erythrocytic life cycle, is considered to be the keypointwheretheactivityofandrographolidewas found to be prominent. Protein and nucleic acid synthesisarethekeypointsintheparasitelifecycle, upon which the mechanism of action of this compound relies. The efficacy of AP solvent extracts as an antibacterial agent in urinary tract pathogenshavebeenreportedbyMurugesan*etal*. (2018).The herb showed an overall effectiveness of 91.3% among patients with acute bacterial diarrhoea after treatment for six days.

Researchers, around the globe attain various leadsbystructurallymodifyingandbrographolide duetothevarietyofbiologicalactivitiesshownby the herb. The pharmacologicalactivities of numerousandrographolidederivativeshavebeen evaluated that have emerged in recent times. A pilot-scaleclinicalstudieshasconfirmedthesafety of the herb. The herb's efficacy against other diseases needs to be evaluated further in all age group populations. However, studies that have comprehensively summarized or analyzed *A. paniculata*and its derivativeshavebeen minimal.Asaprerequisite,thereisaneedfordeep research to assess the potential of the plant in clinical practices. In conclusion, this review highlights the chief eminence of Kalmegh as an established medicinalherb.The various pharmacological activities of the herb make it valuable in ameliorating altered diseases and lay out crucial directions for future research.

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