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A review on phytopharmaceutical importance of asiaticoside

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ABSTRACT

Herbal plant materials have huge potential in the field of medicine, nutraceuticals, perfumery, beverages, fragrances, cosmetics and dyeing industry. *Centella asiatica* (L.) Urban (family: Apiaceae) (*C. asiatica*) is a very popular medicinal herb in Sri Lanka, Madagascar, India and other parts of Asia. Gotu kola, Brahmi and Mandukparniin are the synonyms of *C. asiatica* which is mainly used for improving memory power. The pharmacological importance of *C. asiatica* is mainly because of triterpenes such as asiatic acid, asiaticoside, madecassoside and madecassic acid, *etc*. *C. asiatica* is mainly used for the treatment of mental fatigue, anxiety, epidermal wound, eczema, leprosy, asthma, psoriasis, ulcers and vein diseases. Asiaticoside is a pentacyclic triterpenoid saponin having anti-depression, anti-tumor, anti-inflammatory, anti-oxidant properties and further it also possesses wound healing, antiulcer and anti-hepatofibrotic activities. It improved cognitive impairment in diabetic condition because of the decreased oxidative stress. Quantification of asiaticoside in *C. asiatica* has been done by several methods which were mainly based on high performance liquid chromatography methods using different compositions of mobile phase sand detection systems. In these days scientists are trying to discover novel medicine from natural sources for the development of better drugs. In this review we have collected information of asiaticoside in respect to its medicinal values, pharmacological activities, extraction, isolation, and other analytical aspects. So the present review will be supportive to the scientists who are trying to develop some novel medicines from asiaticoside for the better health prospects.

1. Introduction

Herbs have been used in the field of medicine, nutraceuticals, perfumery, beverages, fragrances, cosmetics and dyeing industry science very early age. More than 40% of drugs used in the world were mainly derived from herbal source. Herbs, vegetables and fruits contain numerous phytochemicals including both primary and secondary metabolites[1]. In the nature we can find different colors, flavors and odors of plants which were mainly because of the presence of plentiful phytoconstituent. These colors, flavors and odors play a very crucial role in the plant's growth, reproduction and defense mechanism against diseases[2]. In India, medicinal practices were mainly based upon herbal medicine, and very huge number of herbs and their products were used for the treatment of various disorders. In the traditional medicine, we can easily find out various prescriptions for different disorders such as wounds, inflammation, skin infections, leprosy, diarrhea, *etc*. A large number of the populations in the world are mainly relying on traditional system of medicines for their primary needs for the treatments of various disorders. Due to structural diversity in the nature, plant based products reveal an important place in the different types of medicines. *Centella asiatica* (L.) Urban (family: Apiaceae) (*C. asiatica*) is a small herb belongs to India, Sri Lanka, South Africa, Madagascar, China, Australia, Japan, Malaysia, *etc*. It is a very popular plant in Asia because of their therapeutic potentials[3-5]. Gotu kola is the synonyms of *C. asiatica* and it is an herbaceous plant which mainly grows in warm-climate countries. It is also known as "Brahmi" in classical Ayurveda and some other common names such as Asiatic Pennywort and Buabok in Thai are also there in the literature. *C. asiatica* is also known as Mandukparniin in Ayurveda comprising more than 50 species. *C. asiatica* plant leaves and preparations are used for improving memory power. The plant

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is the second most exported medicinal species in Madagascar. *C. asiatica* extract is available over-the-counter across the world in the form of different commercial medicinal preparations. Some of the *C. asiatica* based commercial brands marketed are Madecassol®, Centellase® and Blastoestimulina®[6-9]. *C. asiatica,* also known as "Brahmi" in classical Ayurveda, is a herb with unique properties in different systems of medicine. It is used as a brain tonic, further for the treatment of skin diseases, rheumatism and elephantiasis. Rapid regeneration and hairy root culture of *C. asiatica* enhanced production of asiaticoside[10]. Triterpenoid saponins, madecassic and asiatic acid are the important phytochemicals of *C. asiatica*. Asiaticoside promote wound healing and is beneficial in the treatment of leprosy and tuberculosis where as madecassoside showed anti-inflamatory properties. Centellosides have been overproduced through *in vitro* cultures by many researchers due to its medicinal properties[11].

1.1. Bioactive compounds from *C. asiatica*

The beneficial effect of *C. asiatica* are due to various pure phytoconstituents such as madecassic acid, asiatic acid, madecassoside, asiaticoside and and many more which are triterpenes. Concentration of these triterpenes in *C. asiatica* are mainly depends upon its diverse environmental conditions, climatic factors and location. Also, larger leaf contains better amount of triterpenoids. Studies have already proved that *C. asiatica* contains essential oils, amino acids, triterpenoids, asiatic acid, brahmic acid, thankuniside, centoic acid, asiaticoside, centelloside, madecassoside, brahmoside, brahminoside, centellose, terminolic, centic, centellic and madecassic acids[5,12]. The triterpenes isolated from *C. asiatica* are pentacyclic triterpenic acids and other triterpenic glycosides which are of ursane or oleanane type. Out of all the phytoconstituents present in the *C. asiatica*, the most investigated and active constituent is asiaticoside. Flavonoids (quercetin and kaempferol) and some phytosterols (campesterol, sitosterol and stigmasterol) are also reported in the *C. asiatica*. Asiaticoside and madecassoside are the ester glycoside derivatives of triterpenic acid[7,9].

1.2. Medicinal importance of *C. asiatica*

C. asiatica has huge applications in Indian and Chinese system of medicines for anti-aging potential, wound healing activity and neuroprotection. Chemically asiaticoside is triterpene and one of the active phytoconstituents of the *C. asiatica* plant. β-Amyrin synthase and squalene synthase regulate the production of asiaticoside in *C. asiatica* as one of the important factors in the triterpenoid pathway[13]. *C. asiatica* has been used for centuries in India and some other regions for the treatment of disorders such as mental fatigue, anxiety, epidermal wound, eczema, leprosy, asthma, psoriasis, ulcers, vein diseases, in memory improvement, as a antidepressant, antibacterial and antifungal. It also inhibits growth of *Staphylococcus* species and reduces inflammation[6,12]. Animal studies showed that triterpenes in *C. asiatica* have anti-inflammatory properties, wound healing activities and anti-anxiety effects. Many commercial medicinal preparations of *C. asiatica* are available in the market and claimed to be useful for improving venous insufficiency, wound, skin diseases and anxiety[7]. In Ayurveda, *C. asiatica* is mainly used for the treatment of skin tuberculosis, stomach aches, arthritis, leprosy, varicose veins, wound healing, high blood pressure and as memory enhancer. *C. asiatica* extracts also have the antiproliferative effects and protect the venous endothelium. Type I collagen synthesis in human fibroblasts is induced by asiaticoside which changes the gene expression, where as madecassoside has wound healing properties and anti-rheumatoid effect. *C. asiatica* is mainly used in the cosmetic preparations due to the presence of triterpenoids which are mainly used for skin care[8]. *C. asiatica* has been reported to increase protein, total collagen, collagen production, cellular hyperplasia, hexosamine, granulation tissue levels of DNA, cross-linking of collagen and rapid maturation. Study revealed that in human dermal fibroblast cells asiaticoside induced type I collagen synthesis. Topical formulation of *C. asiatica* extract increased collagen synthesis of skin of rats wound due to cellular proliferation. Further wound contraction of the treated wounds epithelialised faster and the rate was also found to be higher. Triterpenes of *C. asiatica* including madecassic acid, asiatic acid and asiaticoside increased collagen synthesis in a dose-dependent manner. In human skin fibroblast cultures triterpenoid fraction influence the biosynthesis of proteoglycans, collagen and fibronectin[4].

1.3. Overview of asiaticoside

Triterpene saponins are one of the abundant classes of phytochemicals present in different taxa of plants and further it is also present in the useful crops like spinach, sugar beets, soybeans and alfalfa. Asiaticoside is triterpene saponins having triterpene aglycone moiety containing one or more than one sugars in its side chains. These unique phytochemicals have hypocholesterolemic, anti-inflammatory, antifungal activities and show contraceptive and foaming properties. Thin-layer chromatography and low-pressure open column chromatography were used for the isolation of saponin where as methanol was also used for the extraction of asiaticoside which was further separated by silica gel column chromatography[14,15]. The most prominent group of biologically active compounds in *C. asiatica* are the triterpenes including asiaticoside, asiatic acid and madecassic. Asiatic acid is an aglycone portion of asiaticoside which is isolated from *C. asiatica* plant[6]. Asiaticoside is triterpenoid saponins with sweet, acrid, and cool taste and is widely used in various systems of medicines as anti-depressant, anti-inflammatory, anti-tumor drug and anti-oxidant. It also inhibits the apoptosis of neural cells, protects nerve cells, improves memory and decreases pain in rat model. Asiaticoside possesses wound healing, antiulcer, anti-hepatofibrotic effects and antioxidant activities. In diabetic condition it improved cognitive impairment and also decreased oxidative stress. Asiaticoside inhibit melanogenesis, a neuroprotector against transient cerebral ischemia and reperfusion[16-18]. Asiaticoside have protective mechanism against chemical-induced hepatotoxicity and further treatment with asiaticoside might induce antidepressant-like effects, and attenuate neurotoxicity in a rat model of Parkinsonism[19]. Quantification of heterosides and various other phytoconstituents of *C. asiatica* have been done with sufficiently validated methods. Several reported methods were mainly based on high performance liquid chromatography (HPLC) methods using different composition of mobile phase and detection system. Quantification of madecassoside and asiaticoside in isocratic mode was performed by the HPLC techniques using acetonitrile/water as a mobile phase. Quantification of asiaticoside, madecassoside, and its isomer has been reported by using evaporative light scattering detector[8].

2. Pharmacological activities of asiaticoside

2.1. Effect of asiaticoside on central nervous system

Asiaticoside derivatives were tested for protective effects against Abeta-induced cell death and showed strong inhibition of Abeta-induced death of B103 cells at 1 microM. The three asiaticoside derivatives were further tested for their effects on free radical injury and apoptosis. All three asiaticoside derivatives reduced H_2O_2-induced cell death and lowered intracellular free radical concentration and among all asiaticoside showed the strongest protection[20]. Fluorescence correlation spectroscopy data analysis showed that asiaticoside inhibited the early stages $A\beta_{1-42}$ of fibrillation, leaving more free Aβs in the solution and permitting their rapid diffusion in the confocal volume. Further molecular docking revealed that asiaticoside binds with amyloid intra- and inter-molecular amino acid residues which are responsible for β-sheet formation and longitudinal extension of fibrils[21]. In another study, Bresnahan, Basso and Beattie scores were evaluated for the determination of the potential activity of asiaticoside on various neurological functions. Asiaticoside significantly improved all the determined parameters in the rat's models. Further the level of water content in spinal cord, nitric oxide synthase, interleukin (IL)-1β and IL-6 and tumor necrosis factor-α were also evaluated in the present rats models and all these data's confirmed the effectiveness of the asiaticoside in the tested models[22]. Effect of asiaticoside on ischemia hypoxia cell was tested for 24 h and further cell survival rate, B-cell lymphoma gene-2, lactate dehydrogenase, Bax, and caspase-3 protein expressions were also measured. From the results it was found that asiaticoside protected *in vitro* ischemia hypoxia neurons[23]. Effect of asiaticoside on oxidative stress and cognition behaviors were investigated in the diabetic rats and it was found that asiaticoside noticeably improved the performance in the Morris Water Maze. Further its effect was also checked in terms of its capabilities of suppressing oxidative stress, protecting hippocampal synapses and restoring Na^+-K^+-ATPase activity[24]. Effect of asiaticoside on depression was evaluated through the activation of brain-derived neurotrophic factor signaling and results showed that mice treated with asiaticoside increased immobility time and inverted the decreased sucrose preference[25]. Effects of asiaticoside in mouse cortical neurons were investigated and results showed that asiaticoside reduce neuronal cell loss in a concentration-dependent manner[26]. Effects of oral administration of asiaticoside on memory impairment and inflammatory cytokines expression were investigated. Results showed that asiaticoside significantly improve the inflammation and memory impairment, signifying the neuroprotective effect against transient cerebral ischemia and reperfusion in mice[27]. Effect of asiaticoside against neurotoxicity in experimental mice was investigated and the results showed that asiaticoside could be effective in protecting neurons from the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine induced oxidative damage[28]. The effect of asiaticoside on the learning and memory abilities in behavioral tests was evaluated and the results showed significance improvement of cognition in senescence-accelerated mice which signified its learning and memory enhancing abilities[19]. Effects of asiaticoside, in the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine induced parkinsonism model were investigated. Results showed that asiaticoside treatment protected dopaminergic neuron through antagonizing neurotoxicity and improved locomotor dysfunction[29]. Forced swimming test, chronic mild stress model and tail suspension test were used to determine the potential antidepressant properties of asiaticoside and result showed that asiaticosid have antidepressant-like potential[30]. Putative anxiolytic activity of asiaticoside was examined in male mice using a number of experimental paradigms of anxiety, with diazepam being as a positive control. In the elevated plus-maze test, asiaticoside increased the percentage of entries into open arms and of time spent on open arms. In the light/dark test, asiaticoside increased the time spent in the light area and the movement in the light area without altering the total locomotor activity of the animals. In the hole-board test, asiaticoside significantly increased head-dipping counts and duration, signifying that asiaticoside exhibited an anxiolytic-like effect[31]. Various parameters were used to assess the anxiolytic activity of asiaticoside, including the elevated plus maze, open field, social interaction, locomotor activity, punished drinking and novel cage tests. The elevated plus maze test revealed that asiaticoside possessed anxiolytic activity[32].

2.2. Effect of asiaticoside on cardiovascular system

Effects of asiaticoside on transforming growth factor β1/Smad signaling were investigated on a hypoxia-induced pulmonary hypertension rat model. From the result it was found that asiaticoside attenuated pulmonary hypertension and pulmonary vascular remodeling in the present tested model[18]. Effect of asiaticoside on endothelial hyperpermeability and disruption of actin filaments in human aortic endothelial cells was investigated. Asiaticoside pretreatment prevented tumor necrosis factor (TNF)-α-induced actin redistribution by suppressing stress fiber formation, and further it also significantly suppressed TNF-α-induced increased permeability[33]. Effect of asiaticoside on lipopolysaccharide (LPS)-induced acute lung injury was evaluated and result showed that asiaticoside treatment attenuated pulmonary inflammation by descended cytokine production, pulmonary edema, reducing inflammatory infiltration and histopathological changes[34]. Effect of asiaticoside along with rapamycin in the inhibition of in-stent restenosis was evaluated and result showed that cell growth inhibition rate in the combination group was significantly higher than the that in individual group for human aortic smooth muscle and fibroblasts cells[35]. Effect of asiaticoside on septic lung injury induced by cecal ligation and puncture in mice were investigated. From the result it was found that asiaticoside significantly decreased the lung pathological damage, total proteins, mortality and infiltration of mononuclear and polymorphonuclear leucocytes[36]. Effect of asiaticoside on acute liver injury induced by LPS/D-galactosamine in mice was investigated. From the result it was found that asiaticoside decreased the elevated hepatocytes apoptosis, aminotransferases and caspase-3 alleviation and also improved the liver pathological injury[37].

2.3. Effect of asiaticoside on skin

Effects of asiaticoside on the proliferation, collagen expression and transforming growth factor of keloid-derived fibroblasts were evaluated and it was found that asiaticoside reduced fibroblast proliferation. Further results suggested that it also inhibited mRNA expressions and type I and type III collagen protein. So from the above results it was concluded that asiaticoside could be used in the treatment of hypertrophic scars and keloids[38]. Effect of asiaticoside on the rabbit ear model of hypertrophic scar was investigated and it was found that asiaticoside alleviated the scar. Further studies also suggested that asiaticoside could decrease transforming growth factor-β1 expression and enhance the expression of inhibitory Smad7[39]. Effects of one of the asiaticoside-containing cream preparation against the periorbital wrinkles of a group of volunteers were investigated for 12 weeks of treatment and result found that most of the periorbital wrinkles were significantly attenuated to some degree, and in the present investigation some female volunteers experienced significant effect on one of their eyes[40]. Effects of asiaticoside on the expression of Smad protein by hypertrophic scar fibroblasts were investigated. Form the data in this study, it was found that asiaticoside markedly enhanced the expression of inhibitory Smad and further it also revealed that asiaticoside could be helpful to induce the Smad7 from the nucleus to the cytoplasm[41]. Effect of asiaticoside in type I collagen synthesis was investigated and it was found that the nuclear translocation of the Smad 3 and Smad 4 complex was induced by the treatment of asiaticoside[42]. In another study asiaticoside was tested separately and in the combined form with some other substances on the skin human fibroblast collagen I synthesis. From the result it was found that in the absence of ascorbic acid it stimulated collagen I synthesis whereas in the presence of ascorbic acid the level of collagen I secretion was found to be higher[43].

2.4. Effect of asiaticoside on wounds

Effect of asiaticoside in both normal as well as delayed-type wound healing in guinea pig was investigated and it was found that asiaticoside increased tensile strength, collagen content, hydroxyproline and significantly increased the epithelisation. Further almost the same results were found in the diabetic animals treated with streptozotocin, signifying that asiaticoside have significant wound healing activity in both normal as well as diabetic animals treated with streptozotocin[44]. Effects of asiaticoside on cytokines production at the site of the burn wound were investigated and from the results it was concluded that topical application of asiaticoside increased vascular endothelial growth factor, monocyte chemoattractant protein-1 and IL-1β levels[45]. Effect of asiaticoside on the antioxidants levels in the wound was investigated and result showed that asiaticoside application in cutaneous wounds increased glutathione peroxidase, superoxide dismutase, vitamin E, catalase and ascorbic acid at an initial stage of healing[46]. Effects of asiaticoside on gastric ulcers induced by acetic acid were examined and result revealed that asiaticoside reduced the size of the ulcers in a dose-dependent manner. Further study also suggested that angiogenesis, expression of basic fibroblast growth factor and epithelial cell proliferation were also promoted[47].

2.5. Effect of asiaticoside on cancer

Effect of asiaticoside against 7,12-dimethylbenz(a)anthracene -induced carcinogenicity were investigated and result showed that asiaticoside treatment increased the caspase-3 activity in MCF-7 cells which signified its effectiveness in both *in vitro* and *in vivo* apoptosis and anti-tumour activity[48]. Effect of asiaticoside in Aβ1-42-induced apoptosis on the human umbilical vein endothelial cell was investigated and results showed that asiaticoside increased cell survival rate and reduced apoptosis, furthermore the expression of Bcl-2 protein was found to be increased whereas the expression of Bax protein was found to be decreased in the asiaticoside treated groups[16]. Effect of asiaticoside on MCF-7 cell uptake of ^{99m}Tc-tetrofosmin and ^{99m}Tc-sestamibi were investiaged and from the result it was found that asiaticoside induce apoptosis and enhance antitumor activity in MCF-7 cells [49]. Effect of angiogenic activity of asiaticoside using chick-chorioallantoic membrane assay was evaluated and result showed the dose-dependent angiogenic activity[50]. Asiaticoside were tested for cytotoxicity on different glioma cell lines such as 1321N1 (Grade II), SW1783 (Grade III) and LN18 (Grade IV) and from the result it was found that asiaticoside had significant activities[51]. Effect of asiaticoside on cytotoxicity and anti-hepatofibrotic activity in HSC-T6 cells, were studied in terms of its configuration relationship. From the result it was found that substitution on the hydroxyl and dihydroxyl groups of the A-ring enhanced the cytotoxicity and anti-hepatofibrotic effect[52].

2.6. Effect of asiaticoside on DNA and enzymes

Inhibitory of effects asiaticoside on human cytochrome P450 (CYP) using recombinant human CYPs *in vitro* were investigated and from the results it was found that asiaticoside inhibited both CYP2C19 and CYP3A4, further data revealed that the above inhibition was found to be non-competitive[53]. Effects of asiaticoside on protection to DNA by gamma radiation under *in vitro*, *ex vivo*, and *in vivo* conditions were investigated and result showed that asiaticoside was found to be effective in terms of protection to DNA from radiation-induced alterations[54]. Effect of asiaticoside on human CYP1A2 was investigated and results showed that asiaticoside did not affect CYP1A2 activity significantly[55]. Effect of asiaticoside on the alternation of genes expression profiles in human dermal fibroblast *in vitro* using cDNA microarray technology was investigated. From the above results it was found that there was a close correlation between the gene profile, mRNA and protein production[56].

2.7. Anti-inflamatory and antipyretic activity of asiaticoside

The effects of asiaticoside on the expression and activity of nitric oxide synthase in gastric ulcer were investigated and result showed that asiaticoside reduced the size of the ulcers in a dose-dependent manner. Further it also attenuated inducible nitric oxide synthase activity and protein expression, signifying its anti-inflammatory property[57]. The anti-inflammatory activities of asiaticoside with other pure phytoconstituents were investigated in LPS-stimulated RAW 264.7 cells and from the result it was found that asiaticoside G significantly inhibited the nitric oxide and TNF-α[58]. The effects of asiaticoside on osteogenic differentiation, proliferation and protein synthesis in human periodontal ligament cells were investigated and result showed the increased levels of fibronectin and collagen type I mRNA and protein in a dose-dependent manner. Further asiaticoside also attenuated matrix metalloproteinase-1 but enhanced tissue inhibitor of metalloproteinase-1 mRNA expression[59]. Effect of asiaticoside in antipyretic and anti-inflammatory activity was investigated and result found that asiaticoside dose-dependently inhibited LPS-induced fever and inflammatory response[60]. Effects of asiaticoside on normal human skin cell behaviors related to healing were investigated. Asiaticoside increased migration rates of skin cells and also enhanced the initial skin cell adhesion. Further in cell proliferation assays, asiaticoside increased the number of normal human dermal fibroblasts[61].

2.8. Effect of asiaticoside on leishmaniasis

Effect of asiaticoside in visceral leishmaniasis which was mainly caused by *Leishmania donovani* was investigated and from the result it was found that asiaticoside had significant activity in animals infected by *Leishmania donovani*[62].

2.9. Effect of asiaticoside on kidney

Molecular mechanism of asiaticoside in treating adriamycin-induced nephropathy of rats was investigated. Synaptopodin, desmin, podocin mRNA, nephrin and protein were determined by RT-PCR and Western blotting. Compared to the untreated nephropathy group, asiaticoside treatment mitigated histological damages, decreased 24-h urine protein excretion and total cholesterol, increased serum albumin. Asiaticoside treatments enhanced the protein levels and mRNA of synaptopodin, nephrin and podocin in a dose-dependent manner[63].

3. Analytical aspects of asiaticoside

The main phytochemicals of Australian *C. asiatica i.e.* asiatic acid, asiaticoside, madecassic acid and madecassoside and other flavonoidal compounds *i.e.* rutin, kaempferol and quercetin and chlorogenic acid were determined through HPLC with diode-array detection method. Further in this study samples for the analysis were collected in different months and from the study it was found that the total content of these triterpenes in January and February month reached its maximum concentration[64]. For the separation of different phytochemicals including asiaticoside from the roots of *Cimicifuga foetida*, high-performance liquid chromatography method with C18 reversed phase silica gel column were used. Further the structures were also elucidated through different spectroscopical and chemical methods[65]. Bioassay-guided screening and chemical analysis of active ethanol extract of *Hydrocotyle sibthorpioides* revealed the separation of asiaticoside[66]. Heptdamoside A, heptursosides A-D, heptoleosides A-D with asiaticoside D and scheffoleoside B, were isolated from the stem barks of *Schefflera heptaphylla* and further their structures were also elucidated through the spectroscopical analysis and other chemical methods[67]. Immunochromatographic strip test has been developed and used for the detection of asiaticoside in *C. asiatica* which is theoretically based upon the monoclonal antibody against asiaticoside[68]. HPLC with pulsed amperometric detector methods used for the determination of asiatic acid, madecassoside, madecassic acid and asiaticoside in *C. asiatica* by the use of Excil ODS 5 mm (C18) column[69]. For the purification of asiaticoside and madecassoside from *C. asiatica*, separation and performance characteristics of several macroporous resins were evaluated and result showed that HPD100 resin separateed madecassoside and asiaticoside[70]. Asiaticoside A and asiaticoside B and other phytoconstituents were isolated from *Actaea asiatica*, and further their structures were elucidated through different spectroscopical methods[71]. An improved qualitative and quantitative method for asiaticoside, asiaticoside-B, madecassoside, madecassic acid, terminolic acid and asiatic acid content in *C. asiatica* was developed and validated by using Phenomenex Aqua 5mu C18 (200 A) column[72]. A new HPLC method is developed and described for the determination of asiaticoside in rat plasma and bile using column-switching and ultraviolet absorbance detection method[73].

4. Plant tissue culture techniques

Effect of *C. asiatica* growth and asiaticoside accumulation under various conditions on centella cell suspension culture was investigated in 5-L bioreactor and result showed that the cell growth and asiaticoside accumulation reached maximum after 24 days of culture. Further result also suggested that asiaticoside content was found to be maximum at inoculum size of 50 g[74]. Effect of production of asiaticoside from *C. asiatica* through *Agrobacterium rhizogenes* and elicitation experiments were investigated. From the result it was found that elicitation and genetically transformed hairy root cultures of *C. asiatica* produced higher amount of asiaticoside compared to the untreated callus[75]. Effect of concentration of nutrient in the growth and asiaticoside accumulation in multiple shoot cultures of *C. asiatica* Urban was investigated. In the present investigation whatever the procedure have been described it provided a good platform for the generation of clean, quality material with high bioactive content from *C. asiatica*[76]. Hairy root cultures were used for the study of various types of secondary metabolites and production and *C. asiatica* hairy roots which were treated with methyl jasmonate could be used for the enhanced production of asiaticoside[77]. Effects of elicitors on asiaticoside production in cultures of *C. asiatica* were studied by the use of different elicitors such as methyl jasmonate, $CdCl_2$, yeast extract and $CuCl_2$. Only methyl jasmonate and yeast extract stimulated asiaticoside production and maximum production of asiaticoside was achieved with 0.1 mmol/L methyl jasmonate[78]. In another study, effect of methyl jasmonate in *C. asiatica* by targeted metabolomic profiling of asiaticoside, madecassoside and their aglycones was investigated in the cell suspension culture[79].

5. Conclusions

Plants and their materials are tremendous source of food, vegetable and traditional drugs, and some of the important drugs which are still used in the different systems of medicines was mainly drawn from from the plant sources. In both developing and developed countries, plant based products have an important role in different systems of medicines. Aspirin, anti-malarial, anti-cancer drugs and many more drugs which play an important role in the modern system of medicine are derived from the natural sources. These herbal derived medicines have been used as one of the best remedies against inflammation, immune system, cardiovascular diseases, blood disorders, cerebral disorders, oxidative stress, *etc*.[80-82]. A large number of the prescribed drugs in the world are mainly derived from the plant sources. More than 80% of the rural population uses medicinal plants and their derived products for the treatment of various disorders[83]. For the determination of identity, purity and strength of the drug phytochemical standards are generally used in the herbal field. These parameters are also used to evaluate its genuine nature compared to the adulterated drugs. Phytochemical evaluation is an important parameter to check the possible steps of adulteration[84]. According to the survey report of the World Health Organization, more than 21 000 plants species are used in the world for the treatments of different disorders[85]. Herbal medicines are gaining popularity in these days due to their fewer side effects and less cost compared to the allopathic medicines. Plants contain both primary and secondary metabolites in the form of various classes of phytochemicals such as carbohydrates, proteins, aminoacids, alkaloids, glycosides, tannins, saponins and many more. Morphine, reserpine, vincristine, vinblastine and quinine, *etc*. are natural derived medicines which are still used in the modern medicine and till so far we don't have any proper substitute for these drugs. For the development of better drugs, in these days scientist are trying to discover some novel medicines from natural sources for the treatment of various disorders as these molecules have various pharmacological activities and have potential to treat different disorders. In this review we have searched out and collected information and summarized the different medicinal values, various pharmacological activities, extraction, isolation, and other analytical aspects of asiaticoside. So the present review will be supportive to the scientists who are trying to discover and develop some novel medicines from the different natural sources for the better treatment of various disorders in the future.

Conflict of interest statement

We declare that we have no conflict of interest.

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