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BIOACTIVE SAPONINS FROM CLEMATIS- MINI REVIEW

Rajeev Rattan
Associate Professor Chemistry, Government College, Haripur, Kangra, HPU-Shimla, India.

ABSTRACT *:* The genus *Clematis* has been a source of various traditionally useful and pharmacologically active species. Many plants of this genus are prominently climbers and woody vines. The species are mosly wild however; few are grown as ornamental plants. The species *Clematis tibtana, Clematis grata, Clematis tangutica*, and *Clematis heraclifolia* were selected to study on their traditional use, chemical composition and pharmacological effects reported in literature. In folklore these species are used as antispasmodic, carminative, diuretic, anodyne, antidote, diuretic and sedative agents. The triterpenoid saponins are the dominant compounds of these species flavonoids, alkaloids, lignans, coumarins, steroids and volatile oils have also been reported from sister spectes. The pharmacological effects evaluated are antioxidant, cytotoxic, antimicrobial, antidiabetic, hepatoprotectve, and anti-inflammatory activities. As such these species has emerged as good source of traditional medicines. The chemical compounds isolated from these species have been reported for their pharmacological effects. Although, few experimental studies validated their traditional claim, but uncharacterized crude extracts were employed in most of the activities. Such species need to be explored properly for their bioactive principle and exploited as potential drug. The review will help the researchers to select medicinally potential species of *Clematis* for future research.

IndexTerms **- *Clematis tibtana, Clematis grata, Clematis tangutica*, and *Clematis heraclifolia*.**

INTRODUCTION

The genus *Clematis* L. (Ranunculaceae) consists of 295 species indigenous in north and south temperate, oceania and tropical African mountains [1]. In India, it is represented by thirty-two species including four sub species and five varieties [2]. The triterpenoids saponins, are the dominant components of this genus. The species are used traditionally for various ailments by the native and nomadic communities. The crude extract and isolated pure compounds possess extensive pharmacological effects such as anti-inflammatory, antitumor, analgesic , anti-inflammatory, arthiritis, antioxidant , antipypretic, antimicrobial, apoptosis, cardio protective and cytotoxic agents comparable to their traditional claim. The extensive study revealed that monodesmodic saponins, flavonoids and alkaloids components present in these species were mainly responsible for most of the biological effects. As a source of herbal medicines for traditional use, chemical constituents diversity and various biological effects the species *Clematis tibtana, Clematis grata, Clematis tangutica*, and *Clematis heraclifolia* were selected for the study. In folklore these species are used as antispasmodic, carminative, diuretic, anodyne, antidote, diuretic and sedative agents. The chemical compounds isolated were saponins, flavonoids, alkaloids, lignans, coumarins, steroids and volatile oils. The present study revealed that hederagenin aglycone based new saponins isolated were 2 from *C. tibtana*, 1 from *C. grata*, 12 from *C. tangutica*, and 1 from *C. graveolens* and oleanane aglycone based were 1 from *C. tibtana*, 3 from *C. tangutica and* 3 from *C. heraclifolia.* The pharmacological activities have been antioxidant, cytotoxic, antimicrobial, antidiabetic, hepatoprotectve, and anti-inflammatory activities. The main objectives of the review are as under;

a) to evaluate the diversity of isolated chemical compounds on the basis of their structural and biological activities.
b) to evaluate whether the traditional use of *Clematis* species has validation in scientific methods in clinical studies.
c) to evaluate whether structure-activity relationship carried out from the isolated compounds.

The data has been compiled using various databases like Google Scholar, Scopus-Elsevier, PubMed, AGRICOLA and Shodhganga. The review will help the researchers to select the species for future investigations.

Traditional uses of clematis species:

Clematis tibtana: The species is native to Nepal, Pakistan, Tibet, West Himalaya, Xinjiang. Clematis tibetana is a deciduous Climber growing to 4 m. The plant scrambles over the ground, climbing into the surrounding vegetation where it attaches itself by means of twining leaf stalks[3]. The stem and flowers are used in Tibetan medicine, they are considered to have and acrid and sweet taste with a heating potency [4]. They promote stomach heat and destroy 'cold tumours'. They are used in the treatment of skin irritations and itches, and tumours [4].

Clematis grata: **Charming Clematis** , the species is native to Afghanistan, East Himalaya, Myanmar, Nansei-shoto, Nepal, Pakistan, Taiwan, Tibet, West Himalaya, India [5]. The plant is grown as an ornamental, often being allowed to grow into trees and large shrubs. It flowers on the current season's new growth and generally does not need pruning unless it is growing too large, in which case simply thinning out some of the stems in late winter or early spring before now growth commences is usually all that is needed. The plant is used as a remedy to treat conditions such as leprosy, blood diseases, and fevers [6]. The stems, or the fibres obtained from them, are used as a tying material [6].

Clematis tangutica (Maxim.) Korsh. – Yellow Clematis, Golden Clematis, Yellow Bower- is a Central Asian species, and is distributed in southeast Kazachstan, Mongolia, western Chinese provinces Gansu, Qinghai, Shaanxi, Sichuan, Xinjiang, in Tibet and Kashmir[7]. In the whole range there are several varieties. This is a decorative species grown in many regions of the world in gardens and parks, unfortunately it easily escapes and can become invasive. In the wild it grows in forests and shrubby slopes, and banks of streams, at elevations from 300 to 4900 m. It blooms from June to August. The whole plants have been used in traditional Tibetan medicine for the treatment of indigestion and invigorating blood circulation [8]. The plant is the main ingredient of Kang Tai capsules, a compound preparation of Chinese herbs, which has showed significant effect in preventing and treating cardiac disease in clinical practice. Previous chemical studies have shown that triterpenoid saponins are the main components of the plant, and the antifungal activities of several saponins were confirmed [9].

Clematis heracleifolia:

Clematis heracleifolia, commonly known as Herbaceous Clematis, is native to China North-Central, China South-Central, China Southeast, Inner Mongolia, Korea, Manchuria [10]. The whole plants play an important role in folk for treating inflammation and tumors. Despite the folk medicinal use of this plant, few chemical constituents and pharmacological assays have been conducted on it. *C. apiifolia*, *C. florida Thunb*. and *C. heracleifolia* DC. (Korea and China) have been traditionally used as analgesic, diuretic, antitumour, and anti-inflammatory agents in Korean traditional system of medicine [11]. *C. heracleifloia* is used as diuretic and antibacterial in China [12].

Chemical constituents from *Clematis* species:

The genus *Clematis* is distributed with wide range of chemical constituents such as triterpenic saponins, alkaloids, flavonoids, coumarins, volatile oils, organic acids, macromolecules, polyphenols etc. The triterpenoid saponins constitute the major class of constituents. The aglycone of *Clematis* species is five-ring triterpenoid oleanane structure (B), 23-OH hederagenin (A), 2, 23-OH Arjunolic acid (C) and quinatic acid (D) (Fig-1). These saponins are both monodesmodic and bidesmodic with glycosylation at Agl C←3 and Agl C←28 except in few cases at Agl C←23. The sugar moieties attached are D-Glucose (Glc), L-Rhamnose (Rha), L-Arabinose (Ara), D-xylose (Xyl), D-Ribose (Rib). The tabulation of saponins is attempted to present in order of increasing oligosaccharide chain on either side. In some cases oligosaccharide chains are also substituted with acetyl, caffeoyl (CA), isoferuloyl (IF), p-methoxy cinnamyl (MC), 3,4-dimethoxy cinnamyl(DMC) moieties. Till date more than 120 new saponins are isolated from Clematis, including 70 oleanane, 50 hederagenin and 2 gypsogenin type [13].

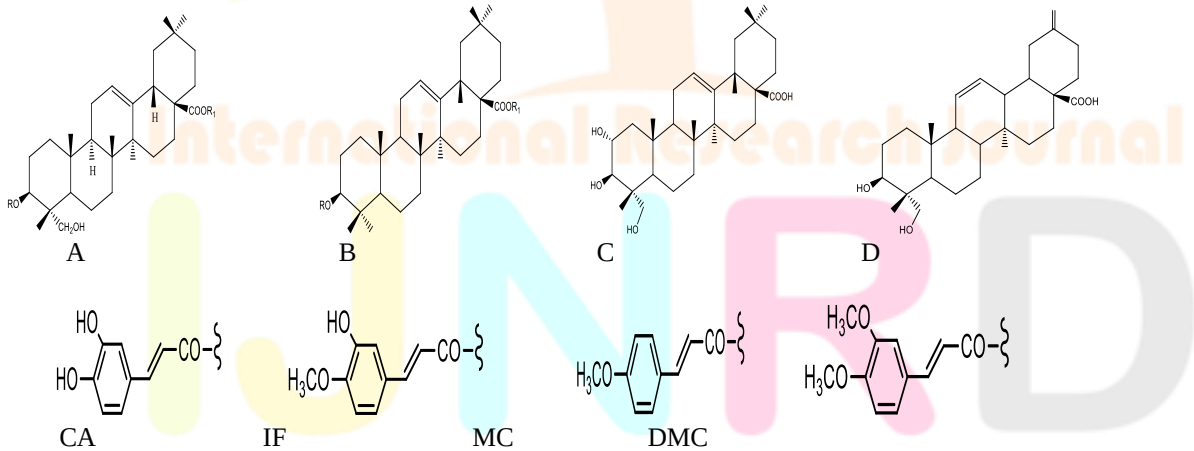

Fig-1 The aglycones from *Clematis*: A-hederagenin, B-oleanane, C-arjunolic acid, D- quinatic acid; moieties-caffeoyl (CA), isoferuloyl (IF), p-methoxy cinnamyl (MC), 3,4-dimethoxy cinnamyl(DMC).

Table-1 Saponins from Clematis species.

Compound	Structure	Source	Ref.
	(Hederagenin Type A)		
Dipsacoside B	R = Rha(1→2)Ara R^1 = Glc(6→1)Glc	*C. tibetana*	[14]
Kizutasaponin K10	R = Ara R^1 = Rha(1→4)Glc(1→6)Glc	*C. tibetana*	[14]
Clematoside S	R = Rib(1→3)Rha(1→2)Ara R^1 = H	*C. grata*	[15]
Tanguticoside A	R = Glc R^1 = Rha(1→4)Glc(1→6)Glc	*C. tangutica*	[16]
Tanguticoside B	R = Glc(1→2)Glc R^1 = Rha(1→4)Glc(1→6)Glc	*C. tangutica*	[16]
Saponin PK	R = Rha(1→2)Glc R^1 = Rha(1→4)Glc(1→6)Glc	*C. tangutica*	[16]
Clematangoticoside B	R=Rha(1→2)Ara R^1= Rha(1→4)Glc(1→6)[Rha(1→2)]Glc	*C. tanguitica*	[17]

Clematangoticoside C	R= H R^1= Rha(1→4)Glc(1→6)[Rha(1→2)]Glc	*C. tanguitica*	[17]
Clematangoticoside D	R=H R^2=Glc R^1= Rha(1→4)Glc(1→6)[Rha(1→2)]Glc	*C. tanguitica*	[17]
Clematangoticoside E	R= H R^2= Glc R^1 = Rha(1→4)Glc(1→6)Glc	*C. tanguitica*	[17]
Clematangoticoside F	R= H R^2= Glc R^1 = Rha(1→4)Glc(1→6)Glc	*C. tanguitica*	[17]
Clematangoticoside G	R= H R^2= Glc R^1 = Rha(1→4)Glc(1→6)Glc	*C. tanguitica*	[17]
Clematangoticoside H	R= Glc[(2←1)Caffeoyl](1→4)Glc(1→4)Xyl(1→3)Rha (1→2)Ara R^1 = Rha(1→4)Glc(1→6)Glc	*C. tanguitica*	[17]
Clematangoside C	R= Rha(1→2)Ara R^1= Glc(1→6)Glc(1→4)Rha(1→4)Glc(1→6)Glc	*C. tanguitica*	[18]
Clematangoside D	R= Rha(1→2)Ara R^1= Rha(1→4)Glc(1→4)Rha(1→4)Glc(1→6)Glc	*C.* tanguitica	[18]
Clematograveo-lenoside A	R= Rib(1→3)Rha(1→2)[Glc1→4)Glc(1→4)]Ara R^1= Rha(1→4)Glc(1→6)Glc	*C. graveolens*	[19]
	Hederagenin 18- en-28-oic acid		
Clematangoside A	R= Rha(1→2)Ara R^1 = Rha(1→4)Glc(1→6)Glc	*C. tanguitica*	[18]
	Hederagenin 21-OH		
Clematangoside B	R= Rha(1→2)Ara R^1 = Rha(1→4)Glc(1→6)Glc	*C. tanguitica*	[18]
	Oleanane		
	(23-CHO Oleanane)		
Clematibtoside B	R=Rha(1→2)Ara R^1 = Rha(1→4)Glc(1→6)Glc	*C. tibtana*	[14]
	(18-en-Oleanane)		
Heracleifolianoside A	R= Rha(1→2)Glc R^1 = Glc(1→6)Glc	*C. heracleifolia*	[20]
Heracleifolianoside B	R = Ara R^1 = Rha(1→4)Glc(1→6)Glc	*C. heracleifolia*	[20]

Nearly, 30 species have been characterized through isolation and structure determination of saponins from *Clematis.* In the present study the hederagenin aglycone based (OH group at C-23 position) new saponins identified from species are 11 from *C. chinensis*, 5 from *C. lasiandra*, 4 from *C. tibtana,* 1 from *C. apiifolia* and 1 from C. graveolens. The oleanane aglycone based (H at C-23 position) (Fig.-1) 11 from *C. chinensis* and 1 from *C. apiifolia* new saponins have been identified (Table-1). Furhtermore, from *C.tibtana* a saponin Clematibtoside B (CHO group at C-23 position) have also been isolated. The sugars and their point of attachment with the sugar chain saponins have large structural diversity. Out of 56 reported saponins, 45 are bidesmodic and 11 are from monodesmodic class. In monodesmodic saponins glycosylation of sugars at (C-3-O←1)Ara(2←1)Rha(3←1)Rib in mostly present however, substitution and further enlargement of chain with glucose, rhamnose and xylose, galactose sugars have also been encountered. Among bidesmodic saponins glycosylation at (C-3-O←1)Ara(2←1)Rha(3←1)Rib and (C-28-O←1)Glc (6←1)Glc(4←1)Rha are commonly observed (Table-1). However, the sugar chains on either side are further enlarged with glucose, rhamnose, galactose and xylose moities.

Table-2 Steroids, Lignans, Coumarins, Macrocyclic, Volite oils from Clematis species.

Compound	Source	Ref.
Alkaloids		
Corytuberine, b-magnoflorine, a-magnoflorine, Me-7-methoxy-3-indolecarbonate, Clemaine	C.erecta, C. mandshurica, C. purpurea	21, 22,23
Flavonoids		
Apigenin, Vitaboside, Kaempferol, Clematine, Hesperetin, Daidzein, Genistein, Luteolin, Quercetin, Rutin, Tangeritin, Isovitexin-6-O-e-p-coumarate, 3,5,7,3' tetrahydroxy flavone	C. viornae L., C. vitalba, C. purpurea , C. armandii, C. hexepetala, C. intricate, C. stans, C. terniflora	24,25,26,27, 28, 29,30
Lignans		
Armandiside, Clemastanin B, (þ)-lariciresino-4-O-β-D-glucopyranoside, Salvadoraside, episyringaresinol, Clemaphenol A, (þ)-pinoresinol , Clemastanin A, Isolariciresinol	C. armandii, C. stans, C. parviloba, C. chinensis C. hexapetala	31,29,33,32, 27
Steroids		
Stigmasterol, Daucosterol, β-sitosterol, β-amyrin, α-amyrin and their glycosides	C. apiifolia, C. hexapetala, C. montana, C. purpurea	34,35,36,23
Coumarins		
4,7-dimethoxy-5-methyl-coumarin, Siderin, Scopoletin	C.delavayi, C. ligusticifolia, C. intricate	37,38,39

Macrocyclic compounds		
Clemoarmanosides A, B, Bercholine, Clemahexapetoside A, B, Clemochinenoside A, B, Ibotanolide B	C. armandii, C. hexapetala, C. chinensis, C. crassifolia	26,35,32,22
Phenolic compounds		
Ibotanolide B, Calceolarioside B, Clemomandshuricoside A, B, C, Tricosanol, Heptacosanoic acid	C.crassifolia,C. mandshurica, C. terniflora	40,22,30
Anemonin, Protoanemonin, Ranunculin	C. angustifolia, C. apiifolia, C. flammula	42,34,41
Volatile oils		
Palmitic acid, Myristic acid, Decasanoic acid, Para-coumatic acid, Caffeic acid, Ferulic acid, 3-hydroxy-4-methoxy benzaldehyde, Inositol, Coniferaldehyde, Vanillin, Pluchoic acid, Protocatechualdehyde, Caffeic acid	C. angustifolia, C. armandii, C. delavayi, C. crassifolia, C. hexepetala, C. montana	42,30,37,40, 35,43

The clematis species has been subjected to isolate various biologically active compounds other than saponins. The alkaloids - phenanthrene, indolecarbonate and clemaine from *C.erecta, C. mandshurica* and *C. parviloba*. The flavonoids from Clematis species are mainly flavonols, flavones, isoflavones, flavanones, xanthones and their glucosides, the aglycones of which are mainly apigenin, kaempferol, luteolin and quercetin. The lignans from *Clematis* are mainly eupomatene lignans, cyclolignans, monoepoxylignans, bisepoxylignans and lignanolides from *C. viornae L., C. vitalba, C. purpurea, C. armandii, C. hexepetala, C. intricate, C. stans, C. terniflora*. Steroids - stigmasterol, β-sitosterol, α, β-amyrin and their glycosides. Macrocyclic compounds- clemoarmanosides, bercholine, clemahexapetoside Clemochinenoside, Ibotanolide from *C. armandii, C. hexapetala*. The volatile oils- palmitic acid, myristic acid, caffeic acid, ferulic acid, inositol, coniferaldehyde, vanillin, pluchoic acid, protocatechualdehyde, caffeic acid mainly from *C. armandii, C. delavayi, C. crassifolia,*

C. hexepetala and *C. montana* (Table-2).

Pharmacological effects of clematis species-

Clematis grata:

Antibacterial activity- The acetone, distilled water and methanol extract of C. grata were examined using Agar-well diffusion method. The methanol extract of leaf showed remarkable antibacterial activity against all the tested bacteria with maximum ZOI against *Staphylococcus aureus* (19.33±1.18 mm) and minimum ZOI against *Salmonella typhi* (12.33±0.26 mm). Also, acetone extract of leaf of this plant was found to be most active against same bacterium *S. aureus* (ZOI=13.66±0.26 mm). Distilled water extract was not active against *S. typhi* and *Escherichia coli*. The methanol extract of root displayed remarkable antibacterial activity against all the tested bacteria with ZOI of 17.00±0.47, 16.00±0.82, 13.00±0.46 and 10.66±0.26 mm against *Bacillus cereus, S . aureus , E. coli* and *S . typhi*, respectively. The rest of the two extracts namely acetone and distilled water displayed no appreciable antibacterial activity against the tested bacteria. Acetone extract of stem showed ZOI of 8.66±0.27, 9.33±0.27, 13.66±1.44 and 16.66±15.66 mm from concentrations 25, 50, 75 and 100% respectively in case of B. cereus[44].

Antioxidant activity: The antioxidant activity for acetone, distilled water and methanol extracts of different parts (leaf, root and stem)of C. grata. Ascorbic acid was used as a standard exhibiting IC_{50} value of 28.12µg/mL Table 2.1. In case of leaf, out of all the extracts, methanol extract exhibited maximum percent inhibition with lowest IC_{50} value of 11.55µg/mL followed by acetone extract with IC_{50} value of 22.59 µg/mL and distilled water extract with IC_{50} value of 56.85 µg/mL table 2.2. In case of root, methanol extract had IC_{50} value of 38.73µg/mL while IC_{50} value of root extract prepared in acetone was 49.01µg/mL. Stem methanol extract had IC_{50} value of 11.39 µg/mL whereas acetone extract had IC_{50} value of 15.75 µg/mL and distilled water extract had IC_{50} value of 34.48 µg/mL[44].

Clematis tengutica

Cytotoxic activity- The cytotoxic activities of the isolated saponins (all the purities > 95%, analyzed by HPLC) against SGC-7901 (human gastric carcinoma cell line), HepG2 (human liver hepatoma cancer cell line), HL-60 (human promyelocytic leukemia cancer cell line) and U251MG (human glioblastoma cancer cell line) were determined according to the MTT method. Adriamycin (98%, Sigma, USA) was used as a positive control against SGC-7901, HepG2, and HL-60 cells, and nimustine (98%, Sigma, USA) was used as a positive control against U251MG cell. The tested saponins (0.5, 2, 10, and 50 mM), adriamycin (0.05, 0.2, 0.5, and 1 mM), and nimustine (0.1, 0.5, 1, and 2 mM), were added into triplicate wells, and were incubated for another 72 h. The plates were at 570 nm on a microplate reader. Saponins possessing a free carboxylic group at C-28 exhibited moderate cytotoxicity against all of the test cancer cell lines with the values of IC_{50} in the range of 1.88e27.20 mM, while saponins 4 and 6 showed selective cytotoxicity against PC-3 with the IC_{50} values of 24.14 and 21.35 mM, respectively. The other tested saponins were inactive (IC_{50} > 50 mM) against the test cancer cell lines. All isolated saponins were inactive (IC_{50} > 50 mM) to the normal human hepatocyte cell line (L02). Clematangoticosides D-G found to be unusual 23, 28-bidesmosidic glycosides. Clematoside S, sapindoside B, kalopanax saponin A, and koelreuteria saponin A exhibited cytotoxicity against all of the test cancer cell lines with IC_{50} values in the range of 1.88e27.20 mM, while clematangoticoside D and F showed selective cytotoxicity against SGC-7901 with IC_{50} values of 24.22 and 21.35 mM, respectively [45].

Antifungal activity- The triterpene saponins isolated ethanol extract of aerial part of *C. tangutica* namely- 3-O-α-L-arabinopyranosyl hederagenin 28-O-α-rhamnopyranosyl ester(1) and 3-O-β-D-glucopyranosyl-(1→4)-α-L-arabinopyranosyl hederagenin 28-O-α-rhamnopyranosyl ester(2) showed antifungal activities against seven fungal strains- *Candida albicans, Candida glabrata, Saccharomtces cerevisiae, Cryptococcus neoformans*,and *Trichosporon beigelii* and plant pathogenic fungus *Pyricularia oryzae* using Agar Diffusion Assay. The amphotericin B was used as positive control. The compounds 1 and 2 showed antifungal activitie with MIA= 2.5 µg/disc against *S. cerevisiae*, simillar to control (amphotericin) and ordinary activity MIA= 10 µg/disc against *P.*

avellaneum, C. glabrata, T. beigelii and *P. oryzae*. The activity observed for the compounds showed that with increasing sugar moiety compound 2 was better antifungal than1 [46].

Anti-Myocardial Ischemia Activity- From the n-BuOH fraction (120 g) of the air-dried and powdered whole plants (3 kg) extracted with 70 % EtOH of *C. tangutica*, the compounds isolated were namely-Clematangoside A, Clematangoside B, Clematangoside C, Clematangoside D, leontoside, cauloside D, kizutasaponin K_{12}, clematibetoside C, hederacholichiside F, and asperosaponin VI. The anti-ischemic activities of saponins 1-10 (all the purities > 96 % analyzed by HPLC) were evaluated by measuring theserum levels of LDH and CK‑MB in hypoxia-treated cardiomyocytes, using diltiazem hydrochloride injection (10 mg/vial, > 98 %) as positive control. Cells were pretreated with various concentrations of saponins 1-10 and diltiazem hydrochloride injection for 24 h and then subjected to hypoxia condition for 3 h. The CK−MB and LDH levels were determined spectrophotometrically at 660 nm and 340 nm, respectively, using diagnostic kits. All saponins were evaluated for their protective effects in hypoxia-induced myocardial injury model. Compounds Clematangoside B, Clematangoside C, Clematangoside D, cauloside D, and asperosaponin VI exhibited anti-myocardial ischemia activities with ED_{50} values in the range of 75.77-127.22 μM [47].

Cardioprotective activity- The air-dried powders of the whole plants of *C. tangutica* were extracted with 70% ethanol. The cardioprotective activities of compounds 1-7 were evaluated by measuring the levels of CK-MB and LDH in A/R treated cardiomyocytes, using diltiazem hydrochloride injec-tion (10 mg/vial,) as positive control. Then cells were incubated in normal culture medium for 6 h in CO_2 incubator. The CK-MB and LDH levels were determined spectrophotometrically at 660 nm and 340 nm, respectively; The results showed that all of these compounds at a concentration of 0.05 mM displayed decreasing effects of the serum CK-MB and LDH levels compared with the A/R group. Compound kalopanaxsaponin G possessed a free hydroxyl group at C-3 and was more potent than the other bisdesmosidic saponins. This suggested that the presence of a free hydroxyl group at C-3 played an important role in terms of cardioprotective activities. The results showed that those saponins exhibited cardioprotective effects by decreasing the levels of creatine kinase-MB (CK-MB) and lactate dehydrogenase (LDH) [48].

Clematis heracleifolia:

HIV-1 protease inhibitor activity-

The methanolic extract of whole plant of C. heracleifolia (20mg/100ml) was subjected for the screening of anti-HIV-1 activity using MT-4 cell line. The extract aws active for inhibitory activities on essensial viral enzymes reverse transcriptates (RT and RNase H activities). Reverse transcriptates and PR heve been important for viral replicati on and promising targets for finding anti-HIV agents. At the contration of 100 μg/ml extract had inhibitory effects of RT= 14.6 ± 9.1, RNase = 16.8 ± 6.3 and protease = 45.3 ± 2.7. The clematis species contain oleanolic acid responsible for significant inhibitory effects of HIV protease [49].

Conclusion

Out of 355 species of genus *Clematis (Ranunculaceae)* 30 species have been systematically characterized for their chemical constituents. The constituents identified from *Clematis* species are flavonoids, triterpenoid saponins, lignans, steroids, polyphenols, and coumarins. Few compounds, especially flavonoids and alkaloids also possess strong evidence of biological importance but no systematic work has been carried out to validate pharmacological activities responsible for bioactive principles. The triterpenoid saponins are mainly of interest of this genus as these are most potent compounds responsible of most of activities. In literature, 26 species are reported in traditional use for the treatment of various ailments like gout, dysentery, rheumatism, analgesic, antitumor, antibacterial, diuretic, anticancer, antimicrobial, anti-inflammatory, arithritis, hepatoprotective, osteoarthritis and HIV-1 protease inhibitors activities. The chemical constituents isolated were hederagenin and oleanane aglycone based saponuns, flavonoids, alkaloids, lignans, coumarins, steroids and volatile oils. The present study revealed that hederagenin aglycone based new saponins isolated were 2 from *C. tibtana*, 1 from *C. grata*, 12 from *C. tangutica*, and 1 from *C. graveolens* and oleanane aglycone based were 1 from *C. tibtana*, 3 from *C. tangutica and* 3 from *C. heraclifolia.* The pharmacological effects reported have been antioxidant, cytotoxic, antimicrobial, antidiabetic, hepatoprotectve, and anti-inflammatory. In most of activities crude extract was used to evaluate these activities. Being a potential folklore medicine and pharmacologically active species clinical studies are needed to establish biological alternatives to synthetic drugs. In lieu of these observations, it is suggested that the research is needed:

(i) to validate more *Clematis* species of traditional uses with pharmacological effects.
(ii) to characterize and isolate bioactive constituents as per market need.
(iii) to investigate more *Clematis* species for isolation of compounds and their mode of actions.
(iv) more clinical studies to establish structure -biological activity relationship.

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