Journal of Pharmacognosy and Phytochemistry

Available online at www.phytojournal.com

E-ISSN: 2278-4136
P-ISSN: 2349-8234
www.phytojournal.com
JPP 2022; 11(4): 263-272
Received: 11-05-2022
Accepted: 16-06-2022

Suguna M
Department of Biotechnology, University of Mysore, Manasagangotri, Mysore, Karnataka, India

Umesha S
Department of Biotechnology, University of Mysore, Manasagangotri, Mysore, Karnataka, India

Corresponding Author:
Umesha S
Department of Biotechnology, University of Mysore, Manasagangotri, Mysore, Karnataka, India

Phytochemical composition, pharmacological properties, and therapeutic activities of genus: *Grewia*

Suguna M and Umesha S

DOI: https://doi.org/10.22271/phyto.2022.v11.i4d.14470

Abstract
Genus *Grewia* belongs to the *Malvaceae* family which has been studied and found to have fabulous therapeutic properties, utilized for the treatment of various diseases. Our ancestors were also seemed to have very good knowledge about this species, because we can find many uses of this plant in the traditional medicinal system like Siddha, Unani, Ayurveda, etc. In these systems, various parts such as fruits were used to treat cardiac, respiratory, and blood issues, root, and bark were used as a demulcent etc. The systematic investigation by researchers on the constituents of this genus, phytochemical analysis and their potentiality has led to the discovery of various properties such as antioxidant, anti-cancerous, antimicrobial, antibacterial, antiviral, antipyretic, analgesic, anti-hyperglycaemic, radio-protective, and enzyme inhibition, etc. In this review, we have attempted to summarize all the studies done on pharmacological and therapeutic properties exhibited by *Grewia* species which are mainly found in India.

Keywords: *Grewia*, pharmacological uses, therapeutic activities, anticancer property, antibacterial activity, antiviral properties

Introduction
India is a country known for its knowledge of traditional medicinal systems like Ayurveda, Unani, Siddha, Naturopathy, Homeopathy, Tibetan, Amchi, Yoga and their applications in health care sector [1]. The approach in these systems is holistic, unlike allopathic system which targets a particular problem [2]. Plant kingdom plays a major role in these systems and is a boon to mankind since it not only takes care of hunger but is the key for maintaining good health of body, mind and soul [3]. There are many medicinal plants such as Neem (*Azadirachta indica*), Turmeric (*Curcuma longa*), and Tulasi (*Ocimum tenuiflorum*) which are known to be very potent and are already in the market as ingredients of many health-related products. Plants with medicinal value have gained a lot of importance because of their potency and safety with which they can tackle not only the underlying disease but also bring other beneficial impacts on the whole body [2]. Since these plants and their products are natural, there is no or minimal side effect and no toxicity caused to vital organs like kidney and liver [4]. This is because it is easy for the body to assimilate and therefore doesn't poses any residual effect too. Another alarming threat we are facing now-a-days in the case of infective diseases is resistance development from pathogens [5]. We have almost reached the last resort for few diseases for which there is an urgent need of finding a new class of antibiotics with a novel mechanism of action. Looking out in nature to address this problem, we might find the best solution and plants are an excellent choice to begin with [6]. Since the constituents of plants are very complex and, they act synergistically with other molecules to combat the pathogens, so it becomes very difficult for the pathogen to emerge with resistance. There is an umpteen number of plants that can be studied for various bioactivities [6]. Systematic survey and rigorous studies may yield many natural products which can prove themselves to be the best. *Grewia* is one such plant genus that has been studied for its various activities across the world and it can be a medical miracle to address many health problems [7]. This plant is found to have many varied phytoconstituents which has proved to be beneficial in treating different ailments like cancer, infectious diseases like malaria, bacterial or viral infections, Alzheimer's disease and diabetes etc. [7].

Phylogenetics
Genus *Grewia* was named in the honor of Botanist Nehemiah Grew, who has the fame of being the father of plant anatomy [7]. *Grewia* belongs to a large flowering plant family *Malvaceae* according to Angiosperm Phylogeny group. Earlier *Grewia* was placed in either *Tiliaceae* or *Sparrmanniaceae* family since it matched the qualities of each genus. When these two genera studied and matched, they were not found to be monophyletic

(all descendants coming from same ancestors) in nature compared to *Malvaceae*. Therefore, these two genera were merged into one family, *Malvaceae* [8].

Scientific classification of *Grewia* is as follows [9]

Kingdom: *Plantae*, Sub Kingdom: *Spermatophyte*, Division: *Angiospermae*, Class: *Dicotyledonae*, Subclass: *Polypetalae*, Order: *Malvales*, Family: *Tiliaceae*, *Malvaceae*, Genus: *Grewia.*

Botanical description

Generally, *Grewia* is either a tree or a shrub. Leaves are nerved between one to nine. Flowers are found to be axillary in most of the species and panicked in some species. Calyx of flowers is composed of distinct sepals which are called aposepalous. Usually, petals in the flower are five in number attached to glands at the base, absent in some species. Numerous stamens present on the raised torus, syncarpous in nature but staminodes are absent. The ovary is placed above the androphore, axile placentation, and fruits are drupe [10].

Harvesting and Production

Grewia species generally bore fruits during the summer season. On an average of 9 to 11 kg of fruits are harvested per tree. Fruits are perishable; so, it must be consumed within a day [11].

Distribution

There are as many as 325 accepted *Grewia* species distributed worldwide and among them, 40 species are found in India [10, 12]. As per the report of the Indian Biodiversity Portal, these species are distributed all over the landscape and forests of India. Every part of this plant species is widely used in many regions to address health problems.

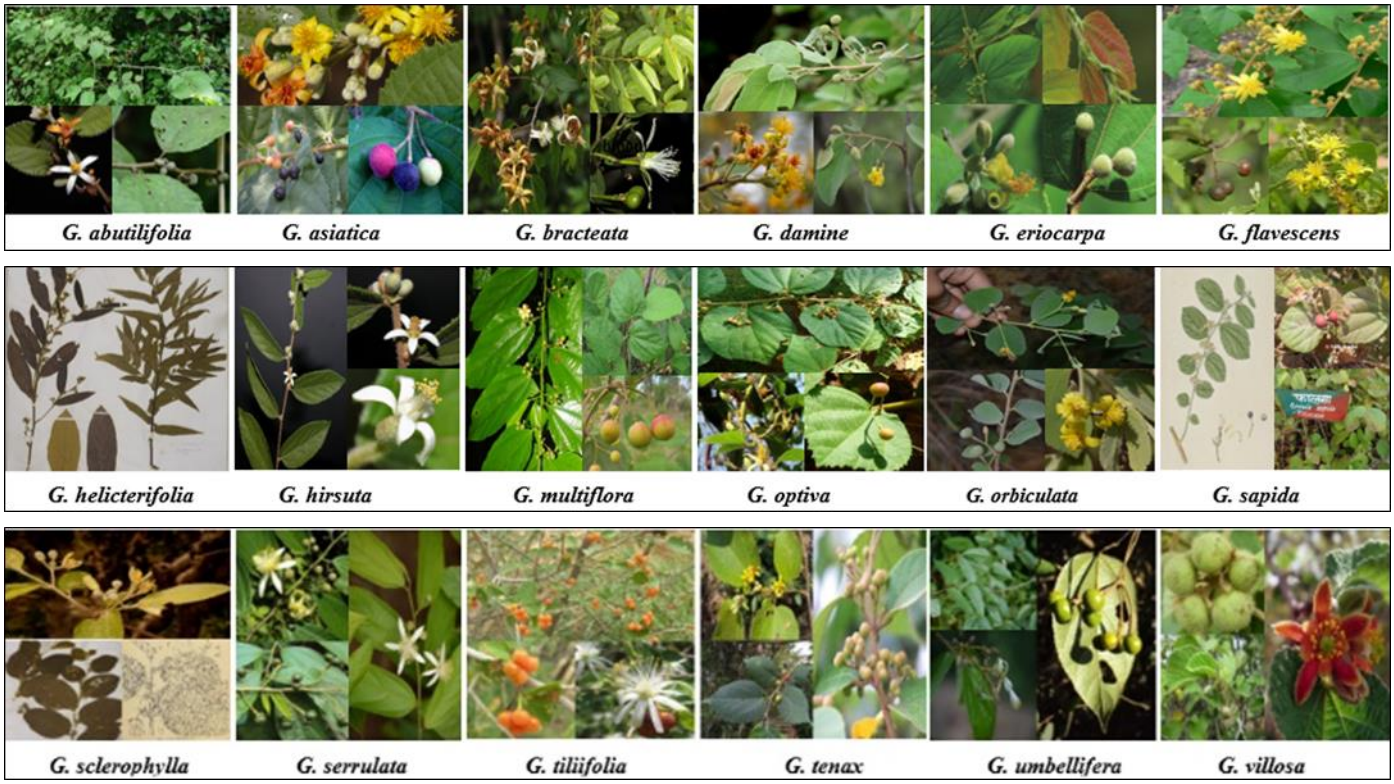


Fig 1: *Grewia* species found in India

Figure 1: Collection of indigenous species of *Grewia* across the nation depicting leaves, flowers and buds of the plants species and their arrangements.

Phytochemical analysis and nutritional value

Species of this genera have great nutritional value and contain many micro and macronutrients. *G. asiatica* (Phalsa) is one such species, which is very well studied and the fruit of this plant is found to be very nutritional with low-calorie index and fat content but high in fibre content. It has Vitamin A such as Thiamine, Riboflavin, Niacin, Vitamin C, mineral salts such as Calcium, Phosphorus, Iron, Potassium, Sodium, and micronutrients such as Cobalt (Co), Chromium (Cr), Copper (Cu), Nickel (Ni), Zinc (Zn) and Iron (Fe) [13].

Phytochemical investigation of the fruit of this plant has revealed the presence of carbohydrates, proteins and amino acids, alkaloids, saponins, steroids, acids, glycosides, mucilage, fixed oils, and fats. It also contains essential amino acids like methionine and threonine, phosphoserine, serine, taurine, aspartic acid, glycine, and tyrosine. Phytochemical analysis of other parts of the plant shows the presence of proteins, mineral salts, sugar, fats, important metabolites like tannins, flavonoids, triterpenoids, phenols, alkaloids, steroids, lignans, lactones, flavones, anthocyanins: cyanidin 3-glucoside, phenols [14, 15].

Another species called *G. abutilifolia* is found to contain valuable phytonutrients such as Saponins, Tannins, Flavonoids, Terpenoids, Steroids, Phlobatannins, Carbohydrates, Coumarins, Alkaloids, Proteins and Emodin [16]. Phytochemical analysis of *G. flavescens* revealed the presence of Flavonoids, Phytosterols, Phenolics, Carbohydrates, Tannins, Triterpenoids and Proteins which are proved to be responsible for the anti-diabetic property [17]. Preliminary analysis of *G. hirsuta* has resulted in a high abundance of phenolics, carbohydrates, alkaloids, flavonoids, and tannins [18]. Phytochemical screening of *G. orientalis* revealing the presence of alkaloids, Tannins, Saponins, Steroids, Glycosides, Terpenoids, Triterpenoids [19]. Similar analysis with *G. sapida* resulted in Alkaloids, Saponins,

Cardiac glycosides, Terpenoids, Anthraquinones, Coumarins, Phenols, Tannins, Flavonoids, Carbohydrates, Starch, Anthocyanins, Proteins, Phlobatannins, Lignin [20].

Important phytoconstituents of *Grewia*

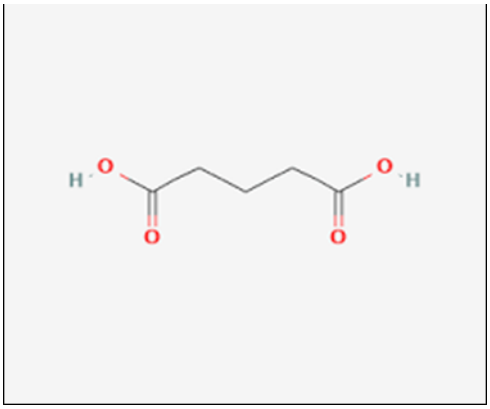
There are many phytochemicals isolated from various species of *Grewia*. The table 1 gives brief information on phytochemicals isolated from this genus.

Table 1: List of Phytoconstituents identified from Genus *Grewia* species

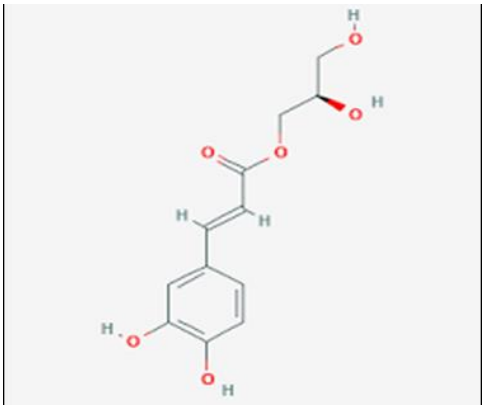
***Grewia* Species**	**Phytochemical**	**Compounds Isolated**	**References**
G. asiatica	Flavonoids	Naringenin-7-O-B-D-Glucoside, Quercetin, Quercetin-3-O-B-D-Glucoside, Naringenin, Kaempferol	[12, 21, 22]
	Anthocyanins	Pelargonidin-3,5-Diglucoside, Delphinidin-3-Glucoside, Cyanidin-3-Glucoside	
	Triterpenoids	Lupeol, Taraxerol, A-Amyrin, B-Amyrin, Lupenone, Erythrodiol, Betulin, Friedelin, B-Amyrin	
	Sterols	B-Sitosterol, Stigmasterol, Campesterol	
	Others	Grewinol, 3, 21, 24-Trimethyl-5, 7-Dihydroxyhentriacontanoic Acid Δ-Lactone, Catechin, Lanost-9 (11)-En-12-One, Docosanol, Nonacosanol, Stigmast-7-En-3-Ol, 9,12-Octadecadienoic Acid Methyl Ester, Citric Acid Trimethyl Ester, A-Methyl-L-Sorboside, Hexadecanoic Acid, Tetradecanoic Acid, 3,4-Altrosan, 4Hpyran-4-One, 2-Hydroxy-3-Methy	
G. damine	Flavones	Vitexin, Isovitexin	[12, 23]
	Triterpenoids	Lupeol, Betulin	
	Alkaloids	Harman, 6-Hydroxyharman, 6-Methoxyharman	
	Sterols	B-Sitosterol, B-Sitosterol-3-O-Glucoside, Daucosterol	
G. flavescens	Triterpenoids	Betulin, A-Amyrin, B-Amyrin, Friedelin, Erythrodiol	[12]
	Sterols	B-Sitosterol	
	Others	Triacontanol	
G hirsuta	Others	(4Z, 12Z)-Cyclopentadeca-4, 12-Dienone	[24]
G. optiva	Coumarins	Scopoletin, Fraxidin	[25]
	Triterpenoids	Lupeol	
	Sterols	*β*-sitosterol, Stigmasterol	
	Others	Grewialin, Optivanin, Grewioptin, Oleanolic acid, Ursolic acid	
G. tenax	Alkaloids	Sedamine	[12, 26]
	Sesquiterpenes	Deterrol Stearate	
	Triterpenoids	A-Amyrin, B-Amyrin, Lupenone, Erythrodiol, Betulin	
	Sterols	Sitosterol, Stigmasterol, B-Sitosterol	
	Others	Triacontanol, Tetratriacont-21-Ol-12-One	
G. tiliaefolia	Triterpenoids	Lupeol, Friedelin, Betulin,	[9, 12, 23, 27]
	Sterols	B-Sitosterol, Stigmasterol	
	Others	Gluconic Acid G-Lactone, D-Erythro-2-Hexenoic Acid G-Lactone	
G. villosa	Alkaloids	Harman	[23, 25]
	Triterpenoids	Ursene-3,19,28-Triol, A-Amyrin, Ursolic Acid,	

Therapeutic properties of some of the phytochemicals found in *Grewia* species

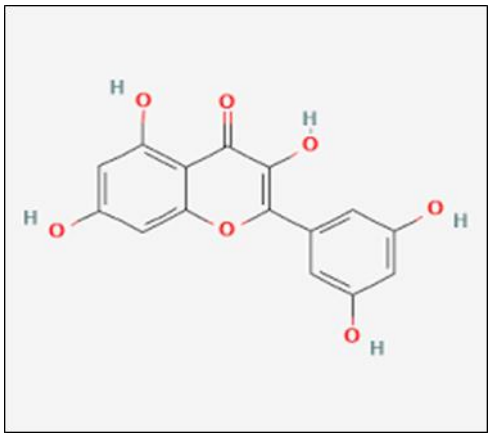
Glutaric acid, 3.4 dihydroxyl phenyl acrylic acid, 2,5 dihydroxyl phenyl) 3',6',8' trihydroxyl-4H chromen-4'-one and Hexanedioic acid found in chloroform and ethyl acetate fractions of *G. optiva* have shown anti-oxidant and anticholinesterase potentials [28]. Lupeol isolated from chloroform extract of stem bark of *G. lasiocarpa* has shown very good biological activities like *in vitro* antibacterial, antioxidant, and cytotoxicity assays. Lupeol at conc. 15-240 µg/mL was found to inhibit growth of pathogenic bacteria such as *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Salmonella typhimurium*, Staphylococcus *aureus* and *methicillin-resistant Staphylococcus aureus*. Also, it was found to have caused cell death in the HEK293, HeLa, and MCF-7 cells [29]. 4Z, 12Z-Cyclopentadeca-4, 12-dienone found in methanolic extract of leaves of *G. hirsute* showed to be the best candidate for developing anti diabetic drug [30]. Kaempferol-3-o-rutinoside and Isorhamnetin-3-O-rutinoside isolated from ethyl acetate extract of *G. tenax* showed antioxidant properties [31]. Vitexin isolated from *G. tiliaefolia* helps in regulating glutamate transporters and protect Neuro2a cells from glutamate toxicity [32]. β-Sitosterol and Daucosterol present in the benzene extract of the leaf of plant *G. tiliaefolia* showed significant anticancer property against A549 cells without causing any harmful effect normal human lung (L132) and PBMC cells [33].



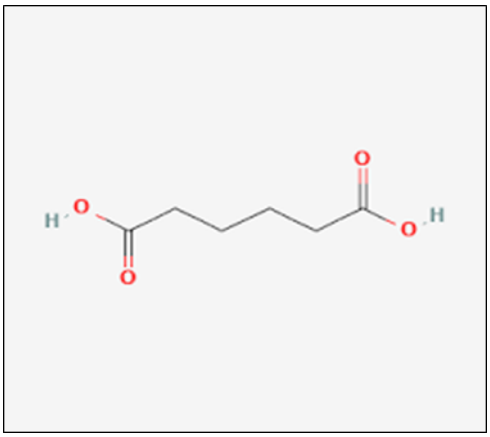
Glutaric acid



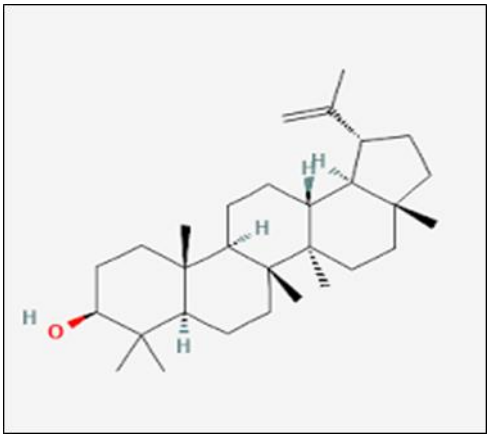
3.4 dihydroxyl phenyl acrylic acid



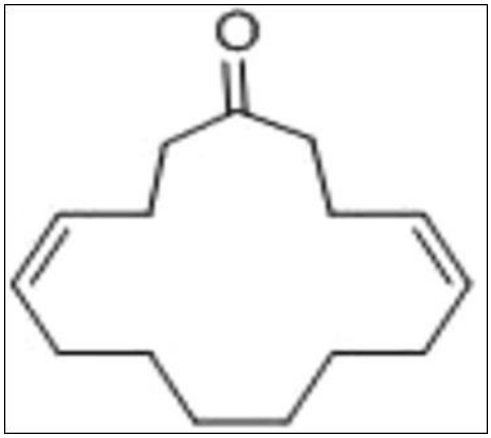
2,5 dihydroxyl phenyl) 3',6',8' trihydroxyl-4H chromen-4'-one



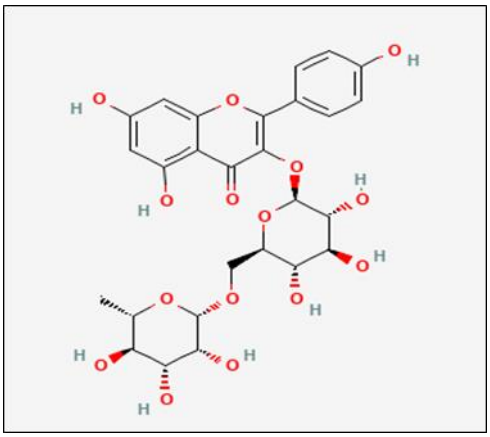
Hexanedioic acid



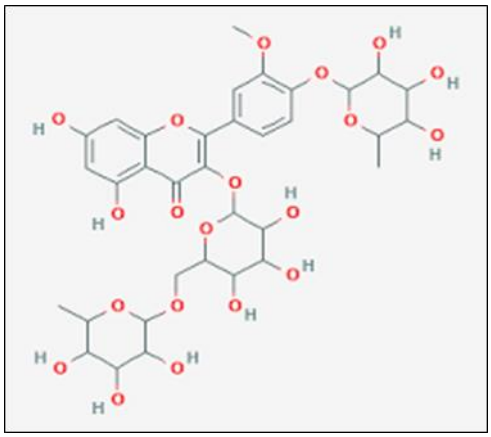
Lupeol



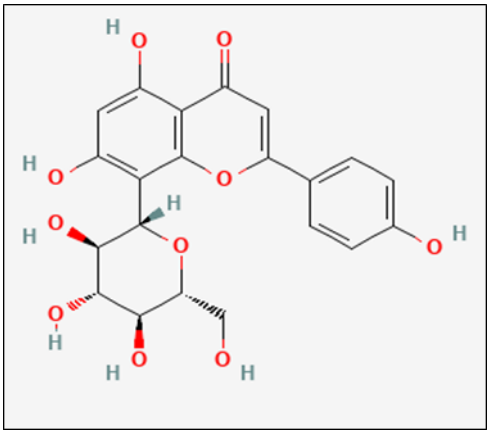
(4Z, 12Z)-Cyclopentadeca-4, 12-dienone



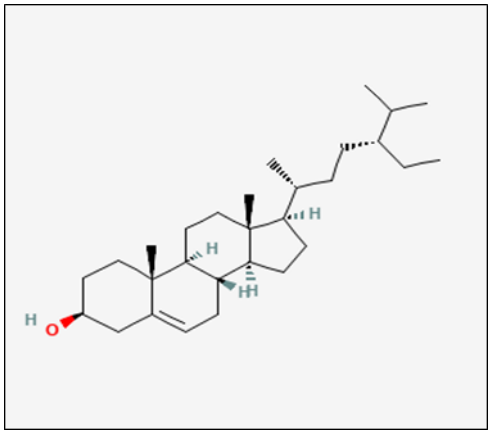
Kaempferol-3-o-rutinoside



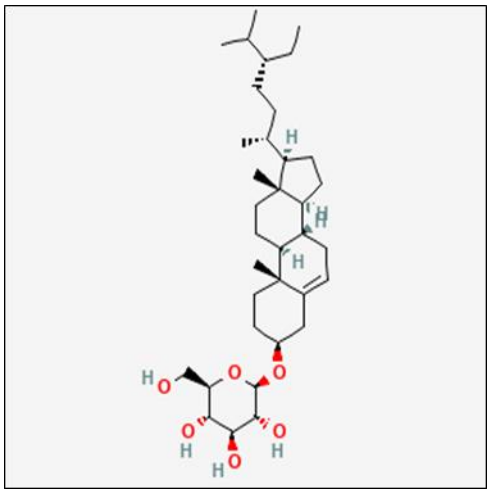
Isorhamnetin-3-O-rutinoside



Vitexin



β-Sitosterol



Daucosterol

Fig 2: Therapeutic phytochemicals identified from *Grewia*

Figure 2: These are some of the prominent secondary metabolites which are found to be having therapeutic activities such as antioxidant properties, antimicrobial properties, and anti-cancerous potency etc.

Traditional uses

The leaves of *G. asiatica* when applied on the skin have beneficial effects like making the skin ejection more connective in addition to anti-toxic properties [11]. *G. asiatica* roots and barks are used for the treatment of stiffness, used as astringent and stomachic, used in case of blood, heart, and respiratory issues [11]. The bark infusion is also used to treat demulcent, febrifuge, and bowel looseness [25]. It is also mentioned in the Ayurveda that the unripened fruit of *G. asiatica* is said to cure *Vata*, *Pitta* and *Kapha* [11]. It also cures aggravation, wound, fever, ulcerative colitis, substantial menstrual stream issues, and diabetes [11, 34]. The fruit alleviates inflammation and is found to be good for throat infections, while it is also used to remove dead foetuses [35].

The traditional medicinal system recommends the use of *G. abutilifolia* plant for the treatment of malaria, smallpox, cough, bladder, and intestine related diseases, eczema, dysentery, typhoid fever, rheumatism, anti-fertility activity and abscesses [16]. Over the years, the tribal people have found a cure for snakebite by consuming a Leaf juice and root bark of *G. gamblei* with other medicinal herbs [18]. The root juice of *G. disperma* has become a common remedy for controlling bleeding, bronchitis, cough and cold among folklore. The bark also finds its use in the treatment for boils while the fruits are used as cardiotonic [36].

The plant *G. tenax* is used in many different ways too. Roots are utilized for treating jaundice, asthma, and pulmonary infections, while leaves are used for trachoma treatment. Leaf decoction and fruit juice are used to boost up haemoglobin count in anaemic patients [26]. Another plant *G. tiliaefolia* finds many uses like treating burning sensation, ulcers and skin-related issues. Leaf and bark decoction is used to treat snakebite, root powder is used in treating sprain [9].

Economical Uses

The ripe fruits of *G. asiatica* are very famous and consumed in the form of juice, squash during summer. The leaves serve as food for animals, the bark is used as a substitute cleanser. While the wood of the tree is proved to be very good material for making bows, shingles, and shafts [37]. Bark fibre acquired is used to make twines [38]. Seeds and leaves of *G. asiatica* are excellent adsorption materials. They, therefore, are used as bio-sorbent for filtering out lead from contaminated water. Fruits of another plant *G. tenax* are widely used in beverages, ice creams, yogurt, and baby food [26]. Crushed bark of *G. tiliaefolia* is used to prevent hair fall [9]. In some countries *G. tenax, G. damine* and *G. villosa* are used as fodder for animals and fruits are consumed by people. Leaves of *G. villosa* are used in beer brewing in Kenya [10].

Pharmacological activities

Antioxidant and anti-diabetic properties

The presence of phytoconstituents in *G. asiatica* such as anthocyanins, lignans, coumarins, flavonoids and isoflavonoids, catechins and iso catechins makes it a good candidate for the treatment of cancer. Cell reinforcement properties of these plants help in treating Alzheimer's disease, stroke, atherosclerosis, and many more which are mainly due to oxidative harm caused by free radicals in the body [39]. According to the study done, the fruits of *G. asiatica* displayed a low Glycaemic Index (GI) index and upon testing showed a beneficial effect on blood glucose metabolism and reactive oxygen species production which makes it worth treating diabetes [40]. When tested in diabetic rats induced by 100 mg/kg of Alloxan monohydrate with dosage 100, 200, and 400 mg/kg of ethanolic leaf extract, *G. flavescens* showed prominent anti-diabetic action [17].

The methanol extract of *G. hirsuta* is found to display free radical scavenging activity along with good antioxidant properties [18]. Ethanolic leaf extract of *G. umbellifera* exhibits antioxidant action in streptozotocin (stz)-induced diabetic rats where it increases the expression of antioxidant enzymes such as glutathione S-transferase (GST), superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPX), glutathione reductase (GR), Glutathione (GSH), Nitric Oxide (NO), etc. and diminishes the levels of lipid peroxides [41]. Hydroxyl, 2,2,1-diphenyl-1-picrylhydrazyl (DPPH) and superoxide radical scavenging assays have revealed the strong antioxidant property possessed by the plants *G. serrulate, G. umbellifera, G. tenax, and G. villosa* [42, 43, 44, 45].

Hepatoprotective nature

Various *in vivo* tests and examinations have been done by different researchers to analyze the radioprotective nature of *Grewia* plants.

Extract of *G. asiatica* is found to exhibit hepatoprotective property. When mice were subjected to radiation, levels of

RNA, DNA and other nucleic acids in the cell are decreased. But when the same irradiated mice were treated with *G. asiatica* fruit concentrate, the level of nucleic acids got regained and there was a tremendous improvement in the concentration of other nucleic acids too. This indicates that *G. asiatica* protects the liver from harmful radiation [46].

Ethylene glycol, a xenobiotic is used to induce hepatotoxicity in mice. After inducing, the animals were fed with 200 mg/kg and 300 mg/kg of *G. hirsuta* leaves syrup extracted with ethanol. Animals treated with ethylene glycol resulted in elevated levels of liver enzymes like Serum glutamic pyruvic transaminase (SGPT) and serum glutamic-oxaloacetic transaminase (SGOT) etc. Consumption of ethanolic extract of *G. hirsuta* resulted in lowering the elevated levels of liver enzymes and also increased the level of proteins which aids in protecting the cells. This proves the beneficial factor of *G. hirsute* extract and its hepatoprotective nature [47].

Ethanolic fruit potions of *G. tenax* showed hepatoprotective activity against CCl_4 induced liver toxicity in Wistar rats. When this potion was fed at dose 250 and 500 mg/kg orally to rats for 21 days, it was found that the CCL_4 induced elevated levels of liver enzymes were reduced. Also, this extract assisted in increasing the haemoglobin level and total protein content in liver tissue [48].

Radioprotective Effect

A study on Swiss albino mice pre-treated with extract of *G. asiatica* has shown protection of the hematopoietic system from harmful radiation. This radiation is known to cause a shortage of blood constituents such as glutathione, sugar, and serum proteins in untreated mice [49].

Yet another study has revealed that fruit mash which was fed at dose 700 mg/kg to gamma radiated swiss albino mice for fifteen days indicated radioprotective action by lipid oxidative degeneration and also observed improved concentration of cerebrum protein and glutathione [50]. The radioprotective nature of *G. asiatica* extract was analysed by exposing pre- and post-treated testis and was compared with the untreated group in male mice. The histological and pathological report revealed that count of spermatocytes, spermatogonia A and spermatogonia B were increased in pre-and post-treated groups when compared to the untreated group [51].

In another experiment, where 700 mg/kg of *G. asiatica* fed orally to mice for 15 days with an exposure of 10 Gy radiation and when the animals were subjected for observation next day, it was found to protect animals from the harmful effect of radiation and showed a reduction in levels of radioactive glutathione (reduced) and increased lipid oxidative degeneration in brain and liver [52].

In a similar study where animals were fed with 700 mg/kg for 15 days and when the effect of radiation was compared between preceding and post-exposure of 5 Gy radiation to the entire body, it was found that implementing *G. asiatica* extract to mice increased alteration in cerebellar lipid oxidative degeneration, levels of glutathione, amino acids and biopsic alterations with $p<0.001$. It also exhibited neuroprotective properties [53]. When the same experiment was done on the intestine, it was found that the intake of fruit extract resulted in a decline in thiobarbituric acid content with an increase in levels of glutathione, protein, and amino acid in testis, and mice cerebrum [50, 54]. It also exhibited a radical displacement of DPPH and oxygen radicals [55].

Anticancer activity

G. asiatica has anti-cancerous activity since it contains many phytoconstituents like vitamin C, anthocyanins and carotenoids. This was proved by conducting MTT (methyl thiazolyl tetrazolium) test on cancerous cell lines namely lung (NCI-H522) and bosom (MCF-7) which resulted in effective IC_{50} values of 59.03 µg/mL and 59.65 µg/mL respectively. Methanolic extract of *G. asiatica* at dose 250 and 500 mg/kg showed anti-cancerous ability when tested against Ehrlich's ascites carcinoma cell lines by increasing the life span of mice bearing EAC by 41% [56]. Methanolic extract of *G. hirsuta* showed a cytotoxic effect on HepG2 cell lines through MTT assay, which indicates the antiproliferative property of the plant [18].

Antifungal Activity

Different leaf extracts of this plant *G. asiatica* have shown antimicrobial activity which has made them useful in treating skin eruptions and psoriasis. Methanolic extract of *G. asiatica* is known to have shown antifungal properties especially against *Candida albicans*, *Aspergillus Niger*, *Aspergillus fumigatus*, *Aspergillus effuses*, *Aspergillus parasiticus*, *Saccharomyces cerevisiae*, *Trichophyton rubrum*, *P. notatum*, and *Penicillium citrinum* [57]. The stem bark extract of *G. optiva* has shown antifungal activity against fungal strains namely *Aspergillus flavus*, *Microsporum canis*, *Fusarium solani* [25]. While Methanolic extract *G. tiliaefolia* shows good sensitivity against *Aspergillus flavus*, *Candida albicans*, and *Microsporum gypseum* [58].

Antibacterial activity

Ethanol extract of *G. asiatica* exhibits antibacterial activity against some of the major pathogenic strains such as *Bacillus subtilis*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Streptococcus pneumoniae*. It also shows similar action against Gram-negative strains which are very difficult to treat otherwise such as *Escherichia coli*, *Proteus vulgaris*, *Proteus mirabilis*, *Salmonella typhi para-A* and *B*, *Shigella dysenteriae*, *Citrobacter* sp., *Pseudomonas aeruginosa*, *Micrococcus luteus*, and *Yersinia aldovae* [58, 59, 60, 61]. Extracts of *G. disperma* also display antibacterial activity against *Escherichia coli*, *Salmonella gallinarum* and *Salmonella typhimurium* [62]. Leaf extract of *G. optiva* shows antibacterial action against *Escherichia coli* and *Pseudomonas aeruginosa* [63].

The killing activity is exhibited by *G. orientalis* when tested against prime pathogens namely *Escherichia coli*, *Bacillus subtilis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia* and *Bacillus thuringiensis* [19]. The stem bark of *G. tenax* exhibits potential killing capacity against pathogen tested namely *Bacillus subtilis*, *Escherichia coli*, *Enterococcus faecalis*, *Staphylococcus epidermidis*, *Salmonella typhi*, *Streptococcus pneumoniae* and *Pseudomonas aeruginosa* [26, 64]. Different solvent extracts of *G. tiliaefolia* are found to have potential inhibitory action of microbes such as *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Enterococcus faecalis*, *Staphylococcus aureus*, *Salmonella typhi A and B*, *Vibrio cholera*, *Klebsiella pneumonia* [58]. Acetone extract of *G. umbellifera* shows good killing potential against *Pseudomonas aeruginosa* and *Staphylococcus aureus* [65].

Antiviral and Antimalarial activity

The antiviral property of this plant was also investigated, and it was found that concentration range of 1000-2000 µg/mL of *G. asiatica* foliage has shown antiviral action against Urdbean Leaf Crinkle Virus (ULCV) and usage of this plant extract in this range has resulted in 90-100% disease control in plants

[57]. The methanolic leaf concentrate of this plant has also shown an antimalarial effect. A test conducted on male chicks at dose 50 mg/kg and 100 mg/kg displayed nauseating action with a percentage of 39.14 and 59.69 respectively [66].

Nematocidal, Larvicidal and Insecticidal activity

The methanol extract of *G. asiatica* leaf shows nematocidal action against *Hemidesmus indicus*, insecticidal action against *Rhyzopertha dominica* and *Tribolium castaneum* and larvicidal property against *Haemonchus contortus* [67].

Phytotoxic and Enterotoxin activity

Methanolic leaf extract of *G. asiatica* shows phytotoxicity against *Lemna minor* and exhibits enterotoxin property against *Artemia salina, brine shrimp* [68].

Antiemetic, Antiplatelet and Anti-inflammatory activity

When there is intrusion or injury caused by a foreign body, there will be neutrophils recruited to check upon these sites and these neutrophils release the content of lysosomes which results in a cascade of signals to alert the body and proteinase, the bactericidal enzymes contained in the lysosomes act to cause inflammation. Further these contents are released to the extracellular region where they cause further tissue damage and inflammation by reacting with the active membrane of tissue. So, anti-inflammatory drugs act by binding to membranes of tissues and alter the surface charge, thereby stabilizing the membrane, in turn protecting from damage [69].

This technique is used to evaluate *in vitro*, to prove the anti-inflammatory effect. Here RBC is exposed to hypotonic sodium chloride solution, which induces haemolysis. The extract which prevents this haemolysis can be considered to cause anti-inflammatory action. N-hexane extract of *G. optiva* used at various concentrations results in the dose-dependent anti-inflammatory property. The best action is shown at dose 50 µg/mL with a percentage of inhibition of haemolysis being 10.68% [69].

The anti-inflammatory effect is also proved *in vivo* by using Carrageenan. This is a mixture of various red algae or seaweed and is highly inflammatory. This is injected into mice to cause inflammation [70]. The usage of this method has shown that the methanol extract of ripped *G. asiatica* fruit has anti-inflammatory action. Edema was created on the paw of rodents by using Carrageenan. When this fruit extract was applied to the edema at a concentration of 250 mg/kg and 500 mg/kg, it resulted in anti-inflammatory action through initiating the healing process [71].

Leaf of *G. asiatica* extracted with alcohol has shown an antiemetic effect in dogs when used at a concentration of 120 mg/kg. Also, when a similar test was done in male chicks, the nauseating action was 39.1% at dose 50 mg/kg and 59.69% at dose 100 mg/kg [72]. Methanolic leaf extract of *G. asiatica* shows antiplatelet activity by inhibiting the platelet aggregation when used in the range 1 to 10 mg/mL with a dose-dependent pattern. This suggests the possible use of this plant in the treatment of cardiovascular or inflammatory diseases [66]. Plant extracts of *G. serrulate* have caused prominent anti-inflammatory and anticoagulant action by inhibiting protein denaturation and stabilizing red blood cells [73]. *G. optiva*, and *G. tiliaefolia* are few other plants which show anti-inflammatory activity [9, 69].

Analgesic and Anti-Hyperlipidaemic Activity

The analgesic property of *G. asiatica* has been analysed using the writhing method or hot-plate technique. In the writhing method, when mice were treated at different concentrations like 100-400 mg/kg, it was observed that 100 to 250 mg/kg showed critical inhibition of pain, 300 mg/kg was on par with ibuprofen whereas 400 mg/kg showed tremendous pain relief effect. Similarly, in the hot plate method, 100 mg/kg showed a remarkable effect, 300 mg/kg showed prominent, whereas 400 mg/kg exhibited an intense inhibitory effect [51].

The leaf extract of *G. asiatica* has been analysed in actuated hyperlipidaemic rats resulting in an anti-hyperlipidaemic effect. When the constituents were analysed, the effect was found to be due to the presence of triterpenes, alcohol, sterols, diterpene. However, the main component which brought this effect was not determined [74]. Even *G. tiliaefolia* has also shown similar activities [9].

Antipyretic activity

Water and methanol extracts of *G. asiatica* are found to have a profound antipyretic effect when tested on mice. The mechanism behind this activity is similar to the known antipyretic substances such as NSAIDs. These act through cyclooxygenase pathway by blocking prostaglandin synthetase, which in turn is responsible for low levels of PGE2 in the hypothalamic region [75]. Antipyretic activity of fruit aqueous extract is also examined in swiss albino mice. Fever is initiated in mice by intraperitoneally injecting 0.01 mg/kg of *E. coli*, whose liposaccharides are removed. This renders *E. coli* passive and mice remain uninfected by the pathogen. Then the rectal temperature was recorded at a regular interval of 30 minutes till 90 minutes. Mice with fever, fed with 300-500 mg/kg of fruit extract showed noticeable antipyretic activity (76). The extract of plants *G. optiva* and *G. tiliaefolia have* also shown this activity [9, 69].

***Acetylcholinesterase* (AChE) and *Butyrylcholinesterase* (BChE) inhibitory activity**

Another study has reported that the extract of *G. abutilifolia* has very good inhibitory activity against *Acetylcholinesterase* and *Butyrylcholinesterase* when tested in comparison with reference standards such as donepezil and galantamine respectively. These two enzymes are considered as the major impact factors of Alzheimer's disease. So, the inhibitory action of *G. abutilifolia* on these factors might prove to be an excellent drug to treat and analyse Alzheimer's disease [16].

Antidepressant property

Feeding Methanolic leaf extract of *G. asiatica* orally at dose 1000, 2000, and 3000 mg/kg to mice. Then numerous tests like forced swimming test, tail suspension test, hole board, hole cross, and open field tests are conducted. These tests showed that the leaf extract has sedative-hypnotic action on these animals. This suggests that the extract influences the central nervous system and acts also as an antidepressant [77].

Immunomodulatory effect

Ethanol extract of *G. asiatica* shows immunostimulant property. When this cocktail was fed to mice at dose 200 and 400 mg/kg, it was observed that it neutralized the effect of cyclophosphamide prompted a decrease in all WBC, Neutrophils and haemoglobin levels and also exhibited increment in phagocytic action by cells [78].

Other properties

Seeds of *G. asiatica* are used as antifertility agents. They are also known to exhibit anti-foetal implantation and so they are considered abortifacient [67]. It is reported that *G. disperma*

has diuretic property [79]. Fruits of *G. optiva* are found to have an astringent quality [69]. Pharmacological survey on plant *G. tiliaefolia* has reported various common properties as that of other species of same genera but also additional special properties like anti-amyloidogenic, wound healing, and neuroprotective properties [9].

Conclusion

Grewia is a worth exploring plant genus scientifically since it has tremendous medicinal value. It has been used by Indian folklore from ages for treating a host of diseases such as stomach upset, fever, cough, inflammation, upper and lower respiratory tract infections, rheumatism, blood disorder issues, etc. Now, researchers have also found beneficial factors such as radioprotective nature, antifertility, anti-hyperglycaemic effect and its ability to treat diseases like cancer, Alzheimer's and diabetes, etc. Scientific research studies have also found that some of the plants of this genus have very good nutritional value along with antimicrobial and antiviral properties. The rich and unique presence of phytoconstituents in different parts of some *Grewia* species such as leaves, fruits, stem, roots, and bark has made the plant a potential source for treating many diseases ranging from the simpler common cold to more complex diseases like Alzheimer's and cancer. This review has mainly focused on the potentiality of genus *Grewia* and how the diversity in its content and possession of various properties are utilized to treat a variety of health issues.

Reference

1. Khanal D, Raut B, Kafle M. A Comparative Study on Phytochemical and Biological Activities of two *Grewia* Species. JMMIHS. 2016;2:53-60.
2. Thakur S, Asrani R, Damu R, Thakur M, Kumar R. Antimicrobial potential of medicinal plants of Himachal Pradesh against pathogenic *Escherichia coli, Salmonella gallinarum* and *Salmonella typhimurium*. Vet. Res. Int. 2018;6(4):67-71.
3. Awuchi CG. Medicinal plants: the medical, food nutritional biochemistry and uses. Int. J Adv. Eng. Res. Sci. Eng. technol. 2019;5(11):220-241.
4. Kuete V. Toxicological Survey of African Medicinal Plant, Elsevier; c2012, p 22.
5. Deepak P, Gopal GV. Preliminary screening of medicinal plants used by Kurumba tribes, Nilgiris district, Tamil Nadu, India. Int. J Med. Plants. 2014;107:502-512.
6. Abreu A, Coqueiro A, Sultan A, Lemmens N, Kim H, Verpoorte R, *et al*., Looking to nature for a new concept in antimicrobial treatments: isoflavonoids from *Cytisus striatus* as antibiotic adjuvants against MRSA. Sci. Rep. 2017;7(3777):1-16.
7. Abujam RD. Nutritional and medicinal properties of phalsa (*Grewia asiatica*) and its therapeutic application- a review. Univ. Res. Reso J. 2018;1(2):226-233.
8. Chung R. Revision of *Grewia* (*Malvaceae-Grewioideae*) in peninsular Malaysia and Borneo. Edinb. J Bot. 2005;62(1-2):1-27.
9. Devi DR, Battu GR. Phytochemical and pharmacological review of *Grewia tiliaefolia* (Vahl.). Int. J Pharm. 2019;10(9):39-42.
10. Pathak A. *Grewia* (*Malvaceae sensu* Lato): ethnomedicinal uses and future potential. Int. J Emerg. Trends Sci. Technol. 2017;4(9):5954-5960.
11. Morton J, Phalsa. In Fruits of Warm Climates. JF Morton Publisher. Miami, USA; c1987, p 352-358.
12. Goyal PK. Phytochemical and pharmacological properties of the genus *Grewia*: a review. Int. J Pharm. Pharm. Sci. 2012;4(4):72-78.
13. Mukhtar HM, Kaur H, Singh S, Singh M. Standardization and preliminary phytochemical investigation of the fruits of *Grewia asiatica* (Phalsa) Linn. J Pharmacogn. Phytochem. 2012;4(4):212-214.
14. Gupta MK, Sharma PK, Ansari SH, Lagarkha R. Pharmacognostical evaluation of *Grewia asiatica* (Phalsa) fruits. Int. J Plant Sci. 2006;1(2):249-251.
15. Sharma PC, Yelne MB, Dennis TJ, Joshi A. Database on Medicinal Plants Used in Ayurveda; CCRAS. New Delhi, India; c2008, p 40-48.
16. Rafe M, Salam R, Hossain M, Masud M. Phytochemical Screening and *Acetylcholinesterase* and *Butyrylcholinesterase* Inhibitory and Thrombolytic Activities of *Grewia abutilifolia* Vent. and Juss. Leaf. Dhaka Univ. J Pharm. Sci. 2018;17(1):81-86.
17. Rama MRM, Yanadaiah JP, Ravindra RK, Lakshman KD, Balamuralidhar H. Assessment of antidiabetic activity of ethanol extract of *Grewia flavescens* Juss. leaves against alloxan induced diabetes in rats. J Glob. Trends Pharm. Sci. 2013;4(2):1086-1090.
18. Dey A, De J. Traditional Use of Plants against Snakebite in Indian Subcontinent: A Review of the Recent Literature. Afr. J Tradit. Complement. Altern. Med. 2011;9(1):153-174.
19. Totakura NP, Vupputuri P, Medaboina G, Neelam S, Chandra BS. Studies on phytochemical and antibacterial activity of methanol, ethanol and acetone extract of *Grewia orientalis* leaves. Int. J Phytomedicine. 2013;5(2):211-216.
20. Islary A, Sarmah J, Basumatary S. Proximate composition, mineral content, phytochemical analysis and *in vitro* antioxidant activities of a wild edible fruit (*Grewia sapida* Roxb. ex DC.) found in Assam of North-East India. J Investig. Biochem. 2016;5(1):21-31.
21. Shukla R, Sharma D, Pathak N, Bajpai P. Comparative Evaluation of Various Flower Extracts of *Grewia asiatica* for Phyto-Compounds and Anti-Bacterial Efficacy. IJBR. 2016;7(4):291-1299.
22. Zia-Ul-Haq M, Stanković M, Rizwan K, Feo V. *Grewia asiatica* L., A Food Plant with Multiple Uses. Molecules. 2013;18(3):2663-2682.
23. Ullah W, Uddin G, Siddiqui B. Ethnic uses, pharmacological and phytochemical profile of genus *Grewia*. J Asian Nat. Prod. Res. 2012;14(2):186-195.
24. Natarajan AN. Isolation and Characterization of (4Z, 12Z)-Cyclopentadeca-4,12-Dienone from Indian medicinal plant *Grewia hirsuta* and its hyperglycemic effect on 3T3 and L6 cell lines. Int. J Pharmacogn. Phytochem. Res. 2014;6(2):393-398.
25. Waliullah, Uddin G, Rauf A, Siddiqui BS, Rehman TU, Qaisar MN, *et al*. Chemical Constituents and Biological Screening of *Grewia optiva* Drummond ex. Burret Whole Plant. Am.-Eurasian J agric. environ. sci. 2011;11(4):542-546. Waliullah, http://prr.hec.gov.pk/jspui/bitstream/123456789/2584/1/3095S.pdf
26. Aadesariya MK, Gauni BM, Duggirala SM, Vijay R, Ram VR, Vyas SJ. Antibacterial activity of Abutilon pannosum and *Grewia tenax* leaves extracts. World J Pharm. Res. 2017;6(16):1259-1274.

27. Badami S, Gupta M, Ramaswamy S, Rai S, Nanjaian M, Bendell D, *et al*. Determination of Betulin in *Grewia tiliaefolia* by HPTLC. J Sep. Sci. 2004;27(1-2):129-131.
28. Ul Bari W, Zahoor M, Zeb A, Sahibzada MUK, Ullah R, Shahat AA, *et al*., Isolation, pharmacological evaluation and molecular docking studies of bioactive compounds from *Grewia optiva*. Drug Des. Devel. Ther. 2019;13:3029-3036.
29. Akwu N, Naidoo Y, Singh M, Thimmegowda CS, Nundkumar N, Lin J. Isolation of lupeol from *Grewia lasiocarpa* stem bark: Antibacterial, antioxidant, and cytotoxicity activities. Biodiversitas Journal of Biological Diversity, 2020;21(12):5684-5690.
30. Natarajan AN. Isolation and Characterization of (4Z, 12Z)-Cyclopentadeca-4,12-Dienone from Indian Medicinal Plant *Grewia hirsuta* and its Hyperglycemic Effect on 3T3 and L6 Cell Lines. Int. J Pharmacogn. Phytochem. Res. 2014;6(2):393-398.
31. Saleh, Ibrahim Flavonoidal. Components, Volatile Constituents and Antioxidant Activity of *Grewia tenax* Forssk. (Tiliaceae) Fruits. Egypt. Pharm. J. 2010;9(2):95-104.
32. Malar MKG, Sharma PK, Ansari SH, Rekha L. Pharmacognostical evaluation of *Grewia asiatica* fruits. Int. J Plant Sci. 2006;1(2):249-251.
33. Rajavel Mesaik MA, Ahmed A, Khalid AS, Jan S, Siddiqui AA, Perveen S, *et al*. Effect of *Grewia asiatica* fruit on glycemic index and phagocytosis tested in healthy human subjects. Pak. J Pharm. Sci. 2013;1:85-89.
34. Lavekar GS. Database on medicinal plants used in Ayurveda and siddha. CCRAS: New Delhi India; c2008.
35. Mahesh KG, Sharma PK, Ansari SH, Rekha L. Pharmacognostical evaluation of *Grewia asiatica* fruits. Int. J Plant Sci. 2006;1(2):249-251.
36. Tuhin M, Asaduzzaman M, Islam E, Khatun Z, Rahmatullah M. Medicinal plants used by folk medicinal herbalists in seven villages of Bhola district, Bangladesh. Am. -Eurasian J Sustain. Agric. 2013;7:210-218.
37. Yadav AK. Phalsa: A Potential New Small Fruit for Georgia Janick (ed). In: J Janick (Ed.). ASHS Press, Alexandria, VA, 1999, 348-352.
38. Paul S. Pharmacological actions and potential uses of *Grewia asiatica*: A review. Int. J Appl. Res. 2015;1(9):222-228.
39. Kumar S, Kumar D. Antioxidant and free radical scavenging activities of edible weeds. African J Food, Agric. Nutr. Dev. 2009;9(5):1174-1190.
40. Mesaik MA, Ahmed A, Khalid AS, Jan S, Siddiqui AA, Perveen S. Effect of *Grewia asiatica* fruit on glycemic index and phagocytosis tested in healthy human subjects. Pak. J Pharm. Sci. 2013;1:85-89.
41. Gunasekaran S, Srinivasan V, Panneerselvam R, Palani S, Evaluation of in-vivo antioxidant effect of ethanolic leaf extracts of *Grewia umbellifera* streptozotocin (stz)-induced diabetic rats. World J Pharm. Res. 2015;4(12):1102-1112.
42. Ramesh M, Rao CB. Antioxidant capacity of hydroalcoholic extracts of *Grewia serrulate* DC and *Grewia nervosa* (lour.) Panigrahi. Int. J Res. Pharm. Sci. 2018;9(1):121-127.
43. Basri SJ, Reddy DG, Jayaveera DK. Anthelmintic activity of crude extract of *Grewia Tenax*. World J Pharm. Res. 2014;3(8):1710-5.
44. Sakthivel S, Sheik AS, Safiullah A. Phytochemical Screening Ethanol Extract of Barks in *Gmelina Arborea* and Grewia Umbellifera. IOSR-JBB. 2017;3(5):22-44.
45. Rao MG, Kumar AO. Antioxidant activity of *Grewia villosa*. J Integral sci. 2018;1(4):12-16.
46. Sharma KV, Sisodia R. Evaluation of the free radical scavenging activity and radioprotective efficacy of *Grewia asiatica* fruit. J Radiol. Prot. 2009;29(3):429-443.
47. Basha SR, Siddapa RD, Jilani D, Kumar GK, Veena V. Preclinical evaluation of hepatoprotective activity of *Grewia hirsuta* extract on ethylene glycol induced liver damage in Wister albino rats. IJRPB. 2015;3(6):2320-3471.
48. Al-Said MS, Mothana RA, Al-Sohaibani MO, Rafatullah S. Ameliorative Effect of *Grewia tenax* (Forssk) Fiori Fruit Extract on CCl4-Induced Oxidative Stress and Hepatotoxicity in Rats. J Food Sci. 2011;76(9):200-207.
49. Singh S, Sharma KV, Sisodia R. Radioprotective Role of *Grewia asiatica* in Mice Blood. Pharmacologyonline. 2007;2:32-43.
50. Ahaskar M, Sharma KV, Singh S, Sisodia R. Post treatment effect of *Grewia asiatica* against radiation induced biochemical changes in brain of Swiss albino mice. Iran. J Radiat. Res. 2007;5(3):105-112.
51. Sharma KV, Sisodia R. Hepatoprotective efficacy of *Grewia asiatica* fruit against oxidative stress in Swiss albino mice. Iran. J Radiat. Res. 2010;8(2):75-85.
52. Ahaskar M, Sharma KV, Singh S, Sisodia R. Radioprotective effect of fruit extract of *Grewia asiatica* in Swiss albino mice against lethal dose of γ irradiation. Asian J Exp. Sci. 2007;21(2):1-14.
53. Sisodia R, Singh S. Biochemical, behavioural and quantitative alterations in cerebellum of Swiss albino mice following irradiation and its modulation by *Grewia asiatica*. Int. J Radiat. Biol. 2009;85(9):787-795.
54. Sisodia R, Ahaskar M, Sharma KV, Singh S. Modulation of radiation induced biochemical changes in cerebrum of Swiss albino mice by *Grewia asiatica*. Acta Neurobiol. Exp. 2008;68(1):32-38.
55. Sharma KV, Sisodia R. Radioprotective Potential of *Grewia asiatica* Fruit Extract in Mice Testis. Pharmacologyonline. 2010;1:487-495.
56. Abidah P, Mohammad I, Muhammad SJ, Kashif W, Meshwish K, Fida M. Lack of brine shrimp lethality and hemagglutination activity in *Grewia asiatica* Linn. J Pharm. Negat. Results. 2013;4(1):1-4.
57. Kumari S, Mazumder A, Pahwa S, Jaju S. Studies of the antifungal and antiviral activity of methanolic extract of leaves of *Grewia asiatica*. Pharmacol. J. 2009;1(3):221-223.
58. Rani TS, Vadivelu A, Chitra K, Reddy CUM. Preliminary phyto chemical screening and antimicrobial activities of *Grewia tiliaefolia* (aerial parts). Int. J Ayurvedic Herb. Med. 2011;1(1):1-7.
59. Siddiqi R, Naz S, Ahmad S, Sayeed SA. Antimicrobial activity of the polyphenolic fractions derived from *Grewia asiatica*, *Eugenia jambolana* and *Carissa carandas*. Int. J Food Sci. Technol. 2011;46:250-256.
60. Israr F, Hassan F, Naqvi BS, Azhar I, Jabeen S, Hasan SMFH. Studies on antibacterial activity of some traditional medicinal plants used in folk medicine. Pak. J Pharm. Sci. 2012;25(3):669-674.
61. Gupta P, Sharma A, Verma AK. GC/MS profiling and antimicrobial effect of six Indian tropical fruit residues

against clinically pathogenic bacterial strain. Int. J Adv. Pharm. Res. 2012;3(10):1229-1235.
62. Kunwar RM, Shrestha KP, Bussmann RW. Traditional herbal medicine in Far-west Nepal: a pharmacological appraisal. J Ethnobiol. Ethnomedicine. 2010 Dec;6(1):1-8.
63. Arora S. Antibacterial, antifungal, antioxidant and phytochemical study on the leaves extract of *Grewia optiva*. J Pharm. Res. 2011;4(9):3130-3132.
64. Ali HA, Salih SA, Ahmed OE, Hamza AA. Biological activity and phytochemical profiling of Grewia Tenax stem bark extracts. Int. J Biol. Pharm. Allied Sci. 2017;6(6):1181-1194.
65. Thirugnanasambandan V, Kannayiram S. Antimicrobial and antioxidant properties of *Grewia umbellifera*. JOHR. 2016;5(2):95-106.
66. Zia-Ul-Haq M, Shah MR, Qayum M, Ercisli S. Biological screening of selected flora of Pakistan. Biol. Res. 2012;45(4):375-379.
67. Jebin R, Molla MI, Mohammad CS, Rafe MR. Antidepressant and sedative-hypnotic activities of methanolic extract of *Grewia asiatica* Linn. leaves in mice. Bangladesh J Pharmacol. 2019;22(2):185-191.
68. Zia-Ul-Haq M, Shahid SA, Muhammed S, Qayum M, Khan I, Ahmad S. Antimalarial, antiemetic and antidiabetic potential of *Grewia asiatica* L. leaves. J Med. Plant Res. 2012;6(16):3087-3092.
69. Anwar J, Shah H, Ali R, Iqbal Z, Khan S, Rahman I, *et al*. Antioxidant activity and phytochemical screening of stem bark extracts of *Grewia optiva* Drummond ex Burret J Pharmacogn. Phytochem. 2015;3:179-182.
70. Hafeez A, Jain U, Sajwan P, Srivastava S, Thakur A. Evaluation of Carrageenan induced anti-inflammatory activity of ethanolic extract of bark of *Ficus virens* Linn. in swiss albino mice. J Phytopharmacol. 2013;2(3):39-43.
71. Bajpai S, Hussain T, Pathak R, Hussain A. Evaluation of anti-inflammatory activity of *Grewia asiatica* methanolic fruit extract in wistar rats. Asian Pac. J Trop. Biomed. 2012;10:1-4.
72. Yaqeen Z, Sohail T, Rahman AU, Saleem M, Rehman ZU. Evaluation of Antiemetic Activities of Alcoholic Extract of *Grewia asiatica* in Experimental Model Dog. Pak. J Sci. Ind. Res. B: Biol. Sci. 2008;51(4):212-215.
73. Usha B, Nandish SKM, Bharadwaj SS, Thejaswi N, Sannaningaiah D, Pushpalatha K. Study on Anti-inflammatory, Anticoagulant, Antiplatelet Activity of *Grewia serrulata* DC. and *Grewia heterotricha* Mast. IJPBS. 2019;9(2):1228-1237.
74. Abou Z, Sleem AA. Anti-hyperlipidemic effect and lipoidal constituents of *Grewia asiatica* (Phalsa) L. leaves. Bull. Natl. Res. Cent. 2005;30:557-573.
75. Gupta D, Rajani G, Sowjanya K, Sahithi B. Screening of Antipyretic activity of aerial parts of Nelumbo nucifera Gaertn. in Yeast induced pyrexia. Pharmacologyonline. 2011;1:1120-1124.
76. Debajyoti D, Achintya M, Debdas D, Achintya S, Jayram H. Evaluation of antipyretic and analgesic activity of parusaka (*Grewia asiatica* Linn.): An indigenous Indian plant. Int. J Res. Ayurveda Pharm. 2012;3:519-524.
77. Jebin R, Molla MI, Mohammad CS, Rafe MR. Antidepressant and sedative-hypnotic activities of methanolic extract of *Grewia asiatica* Linn. leaves in mice. Bangladesh J Pharmacol. 2019;22(2):185-191.
78. Singh S, Yadav AK. Evaluation of immunomodulatory activity of *Grewia asiatica* in laboratory animals. J Chem. Pharm. Res. 2014;6(7):2820-2826.
79. Aswal BS, Goel AK, Kulsheshtha DK, Mehrotra BN, Patnail GK. Screening of Indian Plants for biological activity part XV, Indian J Exp. Biol. 1996;34:444-467.