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# Traditional uses, phytochemistry, quality control and biological activities of genus *Grewia*

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ABSTRACT

*Background:* The genus *Grewia* (Tiliaceae) comprises about 321 species which are distributed in tropical and subtropical regions of the world. They have an excellent medicinal and emergent commercial importance and are traditionally used for the treatment of diabetes, typhoid, hepatitis, diarrhoea, dyspepsia, smallpox, syphilitic ulcers, eczema, malaria, etc. The fruits of *Grewia* species are used as a traditional medicinal diet as a nutraceutical in healthy drinks and food additives. Vitally, in the last decade, the genus *Grewia* has gained more attention due to its diversified traditional medicinal diets along with pharmacological activities. This review aims to provide a complete compilation of comprehensive, systematic, and accurate information on traditional uses, nutritional values, health benefits, phytochemistry, quality control, and pharmacological properties of the genus *Grewia*.

*Method:* All the relevant and systematic literature data on the genus *Grewia* was gathered using multiple electronic databases, including Google Scholar, SciFinder, Web of Science, PubChem, PubMed, ChemSpider, Taylor & Francis, ScienceDirect, ACS Journals, Wiley, Springer, Thieme, The Plant List Database and Scopus. Some other relevant books, book chapters, and Wikipedia are also studied as 'grey literature.

*Results:* The literature survey reveals that the fruits of *Grewia asiatica* and *Grewia tenax* are mainly used for traditional medicinal purposes and are a rich source of nutritional values and bioactive metabolites. About twenty-seven species in the genus *Grewia* have been reported for their pharmacological properties and in which only twelve species have been explored phytochemically. More than 227 chemical compounds, including alkaloids, flavonoids, isoflavonoids, phenols, and volatile classes of compounds have been identified and characterized in twelve species. Flavonoids appeared as the relatively most abundant class of compounds in fruits and could be used for quality control by HPTLC, HPLC, HPLC-MS, and GC-MS. The HPLC-MS methods are comparatively more sensitive than HPTLC and HPLC methods for quality control of raw and finished products based on characteristic compounds. Significant pharmacological activities such as analgesic, anticancer, antidiabetic, antiemetic, anti-inflammatory, antimalarial, antimicrobial, antinociceptive, antioxidant, antiplatelet, antipyretic, hepatoprotective, nephroprotective, neuroprotective, radioprotective, and uterotonic have been reported in methanolic and ethanolic extracts especially leaf extract from twenty- seven species.

*Conclusion:* Conclusive evidence showed that the pharmacological activities of extracts and flavonoids and quality control are supporting and providing confidence in the traditional to modern uses of different products of fruits of *Grewia* species to manage many routine health problems. Based on the existing literature, except *G. asiatica* fruit remains poorly explored, essentially with limited scientific evidence available to support its nutritional and medicinal uses as well as economic benefits. However, this compilation may be short of clear research goals for further study of the *Grewia* species and has a good perspective to develop a new active principle as well as a traditional functional food.

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**Fig. 1.** Photographs of *G. asiatica*; **(A)** whole plants (B) flowers; (C) raw fruits (D) ripe fruits and (E) distribution of genus *Grewia*.

## 1. Introduction

The genus *Grewia* is the most diverse and large flowering genus in the Tiliaceae family with more than 321 described species, which are mostly shrubs and small trees (http://www.theplantlist.org/). The genus *Grewia* is widely distributed all over the tropical and subtropical regions of the world, especially in Asia, Africa, and Australia (Fig. 1). About 31-40 species of *Grewia* are found in Asia, including India, Sri Lanka, and Pakistan. Many reported species of this genus are native to India. Some species are extensively cultivated for fruits and timber in the Asian countries (Haridas et al., 2017; Dev et al., 2019). In India and Pakistan, *Grewia asiatica* L. fruit is edible and commonly known as 'Phalsa or

**Table 1**
Traditional uses of the genus *Grewia*.

| S. No. | Species | Common name | Habitat | Plant part | uses | Preparation | Reference |
|---|---|---|---|---|---|---|---|
| | *G. abutilifolia* | | Shrub | Fruits | bscesses and heumatism | | Joshi et al. (1980) |
| | *G. asiatica* | Phalsa | Shrub | | Stimulate Birth<br>Fracture of bone | Stems boiled with water and given in cattle after birth to promote release placenta<br>Boiled leaves with ajwain taken for easy delivery<br>Root power with water dress in broken bone | Khan & Hanif (2006) |
| | *G. asiatica* | Phalsa | | Ripe fruit | Respiratory, cardiac, blood disorders, diarrhoea, headache, eye complaints, sores, cholera | | Bhakuni et al. (1971) |
| | *G. asiatica* | Phalsa | | Leaves and Ripe fruit | Nose and eye diseases, splenic enlargement, piles, rheumatism relieving joint pain | | Dhawan et al. (1977) |
| | *G. asiatica* | Phalsa | | Ripe fruit | Stomach cooling, Wound healing and rheumatism, Diabetes control, Controlling urinary tract infections, Controlling nausea and vomiting, Fever control, Morning sickness and motion sickness | | Khan et al. (2019) |
| | *G. asiatica* | | | Root bark | Diarrhea, aphrodisiac | Root barks are used. | |
| | *G. flavescens* | Djerma, Gudeim | Shrub | Flower buds | Vegetable | Flower buds are utilized by villagers | Von Maydell (1986) |
| | *G. flavescens* | | | Fruits | Food | Fruits are utilized by villagers and kids | Von Maydell (1986) |
| | *G. helicterifolia* | | | Fruit | indigestion and gastric problems | 1 tablespoon paste of unripe fruits taken twice a day till cure. | Singh & Singh (2015) |
| | *G. tenax* | Gangeti | Shrub | Fruit pulp | Swellings | Fruit pulp from ripe fruit dressed externally on swelled parts thrice a day. | Dev et al. (2017) |
| | *G. tenax* | | | Root bark / Root powder | Dysentery | Root bark powder are boiled with water and taken orally twice in a day. | Dev et al. (2017) |
| | *G. tenax* | | | Root | Female reproductive system problems | Decoction is taken orally. | Dev et al. (2017) |
| | *G. tenax* | | | Leaves | Fever and Hepatitis | The young green leaves boiled in water and decoction is taken twice a day. | Dev et al. (2017) |
| | *G. tenax* | | | Root and leaves paste | Fracture | The root and leaves paste dressed to the fractured area. | Dev et al. (2017) |
| | *G. tenax* | | | Green leaves | Fodder | Green twinges and leaves used as a palatable fodder for goat, cattle and other animals. | Dev et al. (2017) |
| | *G. tenax* | | | Seed and green leaves | Animal delivery | Crushed or paste of green leaves given to animal for easy remove of placenta after delivery. | Dev et al. (2017) |
| | *G. tillifolia* | | Small tree | Wood, leaves and bark | furniture | Wood used furniture and agricultural implements. The leaves are used for fodder while the bark is utilized for fiber and ropes. | Koche (2008) |
| | *G. villosa* | Luska | Shrub | Fruit | Food use | The villagers and kids are eaten ripe fruits. | Dev et al. (2017) |
| | *G. villosa* | Luska | | Dry fruits | Stomach ache | The powder of dried fruit taken with water. | Dev et al. (2017) |
| | *G. villosa* | | | Root | Antidiarrhoeal Cough and body pain | The one-two teaspoons roots powder are mixed in a glass of water and taken orally for diarrhea.<br>Crushed root are boiled in water and decoction taken orally for body pain. | Dev et al. (2017) |
| | *G. villosa* | | | Fruit | Animal delivery | Fresh fruit taken orally after delivery for easy expel of placenta | Dev et al. (2017) |

'Falsa' and has commercial importance due to its nutritive sweet, and sour taste (Khan et al., 2019; Koley et al., 2020; Mehmood et al., 2020) (Fig. 1). *G. asiatica* fruit is acidic and used as healthy, delicious, and refreshing drinks worldwide. The leaves, stem, and root as well as the fruit of *Grewia* species are used as traditional medicines to treat anaemia, cough, diabetes, diarrhoea, dysentery, dyspepsia, eczema, fevers (malaria), heatstroke, hepatitis, itches, typhoid, smallpox, syphilitic ulcers, and wound healing (Dev et al., 2017; Dev et al., 2019; Naqvi et al., 2012; Uniyal et al., 2006; Uddin et al., 2011; Zia-Ul-Haq et al., 2013).

In the past few decades, most of the work has been carried out on the phytochemistry and pharmacology of chemical compounds as well as extracts of plants from the genus *Grewia*. Several phytochemicals such as alkaloids, flavonoids, isoflavones, phenolic acids, lignans, terpenoids, steroids, alkanes, alkenes, alkynes, alcohols, aldehydes, ketones, organic acids, esters, and other volatile compounds have been isolated and identified/characterized in different species (Akwu et al., 2019; Koley et al., 2020; Ma et al., 2006; Meena et al., 2017a; Ullah et al., 2012; Zahoor et al., 2020). The pharmacological studies of chemical

**Table 2**
Nutritional composition of different parts of *Grewia spp*.

| species | g/100 g | | | | | | | | | References |
|---|---|---|---|---|---|---|---|---|---|---|
| | Ash | Carbohydrate | Fibre | Lipid (fat) | Moisture | Protein | Starch | sugar | Unit | |
| *G. asiatica* Fruit | 1.10 | 21.10 | 5.53 | <0.1 | | 1.57 | | | % | Sinha et al. (2015) |
| *G. asiatica* Fruit | 1.10 | 21.10 | 5.53 | <0.1 | 76.3 | 1.57 | | | % | Yadav (1999) |
| *G. asiatica* Seed | 5.08 | 39.74 | 26.16 | 11.19 | | 17.41 | | | (%) | Zia-Ul-Haq et al. (2013) |
| *G. bicolor* Leaves | | | 788.70 | | | 201.9 | | | g/kg DM | Osuga et al. (2006) |
| *G. flavescence* Fruit | 3.40 | 75 | 42.8 | 1.3 | 15 | 3.4 | 38.6 | 10 | % | Elhassan and Yagi (2010) |
| *G. mollis* Leave | 648.6 | | 1,520.36 | | | 533.29 | | | Kg/ha | Saleem et al. (2012) |
| *G. optiva* Fruit | 11.14 | | 21.42 | | 44.85 | 17.32 | | | % | Hashmi and Waqar (2014) |
| *G. populifolia* Fruit | 8.86 | | 27.04 | | 50.31 | 12.58 | | | % | Hashmi et al. (2014) |
| *G. tenax* Fruit | 3.00 | 72.46 | 12.29 | 4.2 | 32.62 | 4.3 | | | % | Aboagarib et al. (2015) |
| *G. tenax* fruit | 3.57 | | | 2.37 | 68.97 | 6.83 | | 32.93 | % | Rathore (2018) |
| *G. tenax* fruit | 3.15 | 66.57 | 14.22 | 0.46 | 7.45 | 8.15 | | 25.5 | % | Abdualrahman et al. (2011) |
| *G. tenax* Fruit | 5.20 | 66 | 20 | 1.7 | 13 | 7.7 | 44.4 | 13.8 | % | Elhassan and Yagi (2010) |
| *G. tenax* Fruit | 3.57 | | | 2.37 | | 6.83 | | 32.93 | % | Rathore (2018) |
| *G. tenax* Peel | | 70.74 | | 1.70% | | 2.12 | | | % | Dev et al. (2017) |
| *G. tenax* Pulp | | 87.09 | | 0.20% | | 3.58 | | | % | Dev et al. (2017) |
| *G. tenax* Pulp | 3.30 | 66.6 | 13.6 | 0.1 | 7.6 | 8.8 | | | % | Abdualrahman et al., (2011) |
| *G. tenax* Seed | | 59.56 | | 10.70% | | 7.21 | | | % | Dev et al. (2017) |
| *G. tenax* Seed | 3 | 66.54 | 14.85 | 0.81 | 7.3 | 7.5 | | | % | Abdualrahman et al. (2011) |
| *G. tenax* Leave | 495.59 | | 1,390.88 | | | 530.77 | | | (Kg/ha) | Saleem et al. (2012) |
| *G. villosa* Fruit | | 84 | | | | 6.7 | 22.8 | 10.4 | % | Dev et al. (2017) |
| *G. villosa* Fruit | 4.00 | 84 | 25.5 | 1.5 | 14 | 6.7 | 22.8 | 10.4 | % | Elhassan and Yagi (2010) |
| *G. villosa* Leave | 537 | | 1,390.88 | | | 530.77 | | | (Kg/ha) | Saleem et al. (2012) |

compounds/ various extracts/fractions of plant parts of genus *Grewia* reported various biological activities such as analgesic, anticancer (cytotoxicity), antidiabetic, antiemetic, anti-inflammatory, antimicrobial, antioxidant, antiplatelet, antipyretic, hepatoprotective, neuroprotective, nephroprotective, and radio-protective functions (Ali et al., 2015; Asuku et al., 2012; Chandiran et al., 2013a; Chandiran et al., 2013b; Gwatidzo et al., 2018; Kubmarawa et al., 2007; Mshelia et al., 2016; Sharma et al., 2007; Shukla et al., 2016; Zia-Ul-Haq., 2012a; Zia-Ul-Haq., 2012b; Zahoor et al., 2020).

Currently, fruits from the genus help in maintaining and managing health problems and have a role in stimulating optimal health conditions, longevity, and the betterment of the quality of life. It show fewer or no side effects and are cost-effective and have proven safe. The World Health Organization (WHO) has approved and appreciated the use of plant-derived medicinal products for various health problems (Chen et al., 2008; Chen et al., 2009; Dhanavath and Prasada Rao, 2017; Pinakin et al., 2020). To maintain the quality of fruits and food products, various well-established sophisticated instrumental techniques are available nowadays. Chromatography-based techniques are more suitable for the analysis of plant- derived products and bioactive marker compounds of a complex matrix like in fruit of plants (Pita-Calvo et al., 2017; El Zahar et al. 2018; Sereshti et al., 2018). Often, successful characterization of a phytochemical can lead to the development of new products or supplements with health-promoting activities. The high-performance thin-layer chromatography (HPTLC), high-performance liquid chromatography (HPLC), high-performance liquid chromatography-mass spectrometry (HPLC-MS), gas chromatography-mass spectrometry (GC-MS) have been widely used based on the nature of compounds in complex matrixes. HPTLC, HPLC, and HPLC-MS are most commonly used for the analysis of non-volatile compounds (Filipiak-Szok et al., 2018; Ristivojević et al., 2019; Stavrianidi, 2020). The liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS) is a widely used analytical tool for the screening of food residues and contaminants. GC-MS is the most suitable technique for analysis of volatile compounds (Al-Rubaye et al., 2017). HPLC-MS is more rapid, sensitive, accurate, and precise than HPTLC, and HPLC for analysis of complex matrix such as plant extracts (Masiá et al., 2016). Several HPTLC, HPLC, and LC-MS methods have been reported for analysis of secondary metabolites from plant extracts of *Grewia* species fruits (Mabika et al., 2017).

Scrutiny of several review articles reveals that most of the literature mentioned only phytochemical and pharmacological properties of *G. asiatica* (Akram et al., 2019; Khan et al., 2019; Mehmood et al., 2020; Paul, 2015; Shukla et al., 2016; Tripathi et al., 2010). However, a review on the genus *Grewia* has been published in which merely thirty-two phytochemicals and eight pharmacological activities have been reported ten *Grewia* species (Zia-Ullah-Haq et al., 2012). Here, this review presents the comprehensive compilation of traditional uses, nutritional value, health benefits as functional food, and chemical compounds with their correlative pharmacological activities in twenty-seven species from the genus *Grewia*. In this perspective, this review also provides the nutritional importance of fruit and its quality control based on bioactive chemical markers by metabolomics approach for standardization of nutraceutical from the plants using HPTLC, HPLC, and LC-MS techniques, with focusing on the need for further research into the health benefits and quality control of this plant.

## 2. Materials and methods

An extensive survey of the previous research on the genus *Grewia* has been collected from all possible print and electronic media, such as Google Scholar, SciFinder, Web of Science, PubChem, PubMed, ChemSpider, NCBI (National Centre for Biotechnology Information), ScienceDirect, The Plant List Database and Scopus. The other relevant books, chapters, and Wikipedia were also studied as grey literature. A combination of keywords was used in the search engine during the literature survey. All the structures of phytochemicals have been drawn using ChemDraw Pro 8.0 software. The PubChem database was checked for an updated international union of pure and applied chemistry (IUPAC) names of chemical compounds reported in the plant. The percentage of contribution of species, plant parts, different types of extracts, and various classes of compounds were calculated using Microsoft Excel 10.

## 3. Traditional uses

The investigation of the literature survey reveals that the leaves, fruit, roots, bark of roots, and stems of plants from *Grewia* are used in folklore medicine for the treatment of multiple disorders like heart, blood, liver and indigestion (Bhakuni et al.,1971; Khan & Hanif, 2006). The ethnomedicinal uses of different plant parts of various species of the genus *Grewia* are presented in the Table 1. Fruits of *Grewia* species are used as a healthy drink, pies, jams, squashes, and chutneys due to their

**Table 3**
Mineral composition in different parts of *Grewia Spp*.

| species | Macronutrients (mg/100 g) | | | | | Micronutrients (mg/100 g) | | | | | | | | | Vitamin | | | | Reference |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Ca | P | Mg | Na | K | Fe | Co | Cr | Cu | Ni | Zn | Pd | Mn | Ni | A | B2 | B3 | C | |
| *G. abutilif* Leave | 10.21 | | | | 0.78 | | | | | | | | | | | | | | Sonawane (2019) |
| *G. asiatica* Fruit | 136 | 24.2 | | 17.3 | 372 | 1.08 | 33 | 36 | 16 | 87 | 48 | | | | 16.11 | 0.264 | 0.825 | 4.385 | Sinha et al. (2015) |
| *G. asiatica* fruit | 136 | 24.2 | | 17.3 | 372 | 140.8 | 0.99 | 0.48 | | 2.61 | 1.44 | | | | 16.11 | 0.26 | 0.82 | 4.38 | Mehmood et al. (2010) |
| *G. asiatica* Fruit | 136 | 24.2 | | 17.3 | 372 | 1.08 | | | | | | | | | 16.11 | 0.264 | 0.825 | 4.385 | Yadav (1999) |
| *G. asiatica* Fruit | 11.2 | | | | 1.51 | | | | | | | | | | | | | | Sonawane (2019) |
| *G. asiatica* Fruit | 820.32 | 294.11 | | 264.01 | 814.56 | 27.1 | | | 1.09 | | 2.04 | | 1.03 | | | | | | Zia-Ul-Haq et al. (2014) |
| *G. damine* Leave | 9 | | | | 1.11 | | | | | | | | | | | | | | Sonawane (2019) |
| *G. flavesce* Leave | 10.85 | | | | 0.70 | | | | | | | | | | | | | | Sonawane (2019) |
| *G. flavescence* Fruit | 269 | | | | 877 | 26.9 | | | 1.1 | | 1.1 | | 0.1 | | | | | | Elhassan and Yagi (2010) |
| *G. nervosa* Leave | 8.9 | | | | 1.28 | | | | | | | | | | | | | | Sonawane (2019) |
| *G. orbicul* Leave | 13.75 | | | | 1.07 | | | | | | | | | | | | | | Sonawane (2019) |
| G. serrulat Leave | 12.1 | | | | 2.4 | | | | | | | | | | | | | | Sonawane (2019) |
| G. tenax Leave | 11.94 | | | | 1.14 | | | | | | | | | | | | | | Sonawane (2019) |
| G. tenax Fruit | 0.33 | 1.05 | 71.1 | 1.5 | 1.26 | 7.95 | | | 0.53 | | 1.98 | | 0.58 | | | | | 45.94 | Rathore (2018) |
| G. tenax Fruit | 790 | | | | 817 | 20.8 | | | 1.5 | | 1.9 | | 5.1 | | | | | | Elhassan and Yagi (2010) |
| G. tenax Fruit | | | | 12.24 | 400.83 | 3.63 | | 0.02 | 0.8 | | | 0.01 | 0.87 | | | | | | Aboagarib et al. (2015) |
| G. tenax Fruit | 0.32 | 1.05 | 71.1 | 1.49 | 1.26 | 7.95 | | | 0.53 | | 1.98 | | 0.58 | | | | | 45.94 | Rathore (2018) |
| G. tenax Fruit | 40 | | | | | 25 | | | | | | | | | | | | | Abdualrahman et al. (2011) |
| G. tenax Peel | | | | 19.32 | 502.5 | 3.25 | | 0.02 | 0.78 | | | 0.01 | 0.62 | | | | | | Dev et al. (2017) |
| G. tenax Pulp | | | | 11.57 | 300 | 4 | | 0.01 | 0.27 | | | 0.015 | 0.28 | | | | | | Dev et al. (2017) |
| G. tenax Seed | | | | 5.82 | 400 | 3.65 | | 0.02 | 1.35 | | | 0.01 | 1.7 | | | | | | Dev et al. (2017) |
| G. tiilifolia Leave | 10.72 | | | | 1.03 | | | | | | | | | | | | | | Sonawane (2019) |
| G. villosa Fruit | 0.40% | | 0.33% | 0.08% | 1.25% | 24.3 | | | 0.46 | | | | | | | | | | Dev et al. (2017) |
| G. villosa Fruit | 536 | | | | 966 | 29.6 | | | 1.2 | | 2.5 | | 0.1 | | | | | | Elhassan and Yagi (2010) |
| G. villosa Leave | 1.0486 | 10.99 | 55.64% | | 88.94% | | | | | | | | | | | | | | Dev et al. (2017) |
| G. villosa Leave | 12.72 | | | | 1.49 | | | | | | | | | | | | | | Sonawane (2019) |
| G. villosa Seed | 0.30% | | 0.18% | 0.02% | 0.0065 | 8.90 | | | 0.39 | | | | | | | | | | Dev et al. (2017) |

protective properties.The plant parts of *Grewia* species are utilized in the form of decoction, juice, paste, powered of plant parts for the treatment of blood, heart, liver disorders as well as anorexia, asthma, cholera, diarrhoea, diabetes, eye complaints, fevers, hiccough, indigestion, piles, thirst, toxemia, stomatitis, and spermatorrhoea, etc. (Dhawan et al., 1977; Khan et al., 2019). The decoction of leaves is used for easy delivery and paste applied to the skin wounds and cuts to relieve irritation and painful rashes. The boiled water extract of the root is used to treat the bone fracture and the root bark used for the treatment of rheumatism and urinary tract problems while diarrhoea and aphrodisiac are cured by the stem bark. The fruits of *Grewia tenax* (Forssk.) Fiori are used to treat swelling and inflammation while a decoction of root barks or roots are used for dysentery, bone fracture and treatment of problems in the female reproductive system. Dry fruits and root of *Grewia hirsuta var. helicterifolia* (Wall. ex G.Don) Haines, *Grewia abutilifolia* Vent. ex Juss and *Grewia villosa* Willd are used in the treatment of stomach ache, abscesses and rheumatism, coughs and body pain whereas *Grewia tilli-ifolia* Vahl is used for the treatment of inflammation. Additionally, leaves and fruits of most of the *Grewia* species are cultivated as fodder for animals, and its stems boiled with water use to promote ease of release of the placenta in cattle when they give birth to a calf. Furthermore, ripe fruits of *G. asiatica, G. tenax, G. villosa*, and *Grewia flavescens* Juss are an important source of raw materials for pharmaceutical, food, and beverage industries. (Cherian & Ramteke, 2010; Dev et al., 2017; Joshi et al., 1980; Koche, 2008; Singh & Singh, 2015; Von Maydell, 1986; Von Maydell, 1990).

### 3.1. Nutritional composition

The protein, fibre, minerals, vitamins and antioxidants rich fruits in routine intake of diet play an important role in maintaining daily healthy life. The fruits are low in calories and fat whereas high in minerals, fiber, protein and vitamin content. The fruits used to add distinctive flavour and deliciousness in health drinks and as a home-based remedy in several health circumstances. The macro and micro nutritional contents (carbohydrate, fibre, fat, moisture, protein, starch, and sugar) of *Grewia* species are compiled in Table 2 and 3. Ash, carbohydrate, fibre, fat, moisture, protein, starch, and sugar were analysed using methods recommended by Association of Official Analytical Chemists (AOAC) (Baur and Ensminger, 1977; González and Herrador, 2007).

#### 3.1.1. Protein

The protein content ranged from protein (1.57-17.41%) on dry weight basis of different parts. A comparative investigation showed that the high protein content has been reported in fruits of *G. asiatica* (17.41%) (Yadav, 1999; Zia-Ul-Haq et al., 2013; Sinha et al., 2015). Approximate, same results have been also reported in *G. optiva* fruit (17.32%). However, significant protein content is reported in G. populifolia fruit (12.58%) (Hashmi and Waqar, 2014). Among the many *Grewia* species, *G. tenax* fruits comparatively more explored than others and various researchers have reported its protein content ranged from 2.12-8.8% (Elhassan and Yagi, 2010; Rathore, 2018). Similarly, *G. villosa* fruit also showed substantial content (6.7%) (Dev et al., 2017). Protein content is comparable with the Guava fruits which are known for their high protein rich content in fruit (Johnston et al., 2006; Yousef et al., 2014).

#### 3.1.2. Dietary fibre

The fibre is the indigestible and important part of fruits and vegetables. It helps keep the digestive system healthy. Elhassan and Yagi, (2010) et al. have determined 42.8 % fibre in G. flavescence fruit (Elhassan & Yagi, 2010). However, good fibre content in fruit of G. populifolia (27.04%) and *G. villosa* (25.50%) and seed of *G. asiatica* (26.16%) was also reported (Zia-Ul-Haq et al., 2013; Hashmi and Waqar, 2014).

#### 3.1.3. Carbohydrate

The carbohydrates are the primary source of energy utilized during metabolism and other activities. *Grewia* fruits contain high carbohydrates. Carbohydrates have been reported in ranges from 21.10-87.09%. Fruits of *G. tenax* and *G. villosa* showed high content of carbohydrate therefore these species may be selected as a source of carbohydrates (Elhassan & Yagi, 2010; Rathore, 2018).

#### 3.1.4. Fat, starch and sugar

*Grewia* species have a low content of fat (0.1-11%), starch (22-44.8%) and sugar (10-32.93%) also. Comparative high fat content has been reported in *G. tenax* seed only (Elhassan & Yagi, 2010).

#### 3.1.4. Moisture and Ash

The moisture is an important indicator of quality and characteristics in consumer sensory perception of food. Ash content is also necessary for nutrition and longevity of a fruit. Most of the fruits from *Grewia* plant contain a good quantity of moisture and ash. The fruits of *G. tenax* fruit and *G. optiva* showed high content of both (Hashmi and Waqar, 2014; Rathore, 2018). Good composition of ash (1.10-8.86%) indicates that it has high mineral content and mineral absorbing power.

#### 3.1.5. Macro and micronutrients

The atomic Absorption Spectrophotometer, Absorption Spectrophotometer and Energy Dispersive X-ray Fluorescence Transmission Emission Spectrometer were used for the elemental analysis of macro and micro nutrients of fruits and leaves of *Grewia* plants. In the *Grewia* averagely each 100 g of fruits contain calcium (Ca) 0.33-820.32 mg/g (essential for bone and teeth, maintaining bone strength, nerve, muscle and glandular function, blood clotting), phosphorous (P) 1.05-294.11 mg/g (used for energy production, phosphorylation process, bone and teeth, for genetic material), magnesium (Mg) 77.10 mg/g (for healthy nerve and muscle function, bone formation), sodium (Na) 0.08-254.01 mg/g (for healthy heart and blood circulation etc.), pottasium (K) 0.70-814.56 mg/g, iron (Fe) 1.08-140.8 mg/g (energy production, Hb, oxygen transport), cobalt (Co) 0.99 and 99 mg/g(component of Vit. B 12 and B 12 coenzymes), chromium (Cr) 0.01-36(with insulin it helps in conversion of carbohydrate and fat into energy, treatment of diabetes), copper (Cu) 0.27-16 mg/g (Hb and collagen production, function of heart, energy production, absorption of iron), nickle (Ni) 2.61 and 87 mg/g, zinc (Zn) 1.1-48 mg/g(essential for cell reproduction, for development in neonates, wound healing, production of sperm and testosterone hormone), palladium (Pd) 0.01 mg/g and manganese (Mn) 1.1-5.1 mg/g content approximately. The content of calcium is comparable with the Ca-rich fruits like orange juice, mulberries, blackberries, guavas, papaya, and passion fruit. The content of iron is much higher than other fruits like spinach. Therefore the fruits from *Grewia* are used as source of iron for our body and can be used as ingredient of regular diet in iron deficiency cases and diseases (Wall, 2006;de Mello Prado et al., 2008; Vinha et al., 2016; Srivastava and Malhotra, 2017; Yuan and Zhao, 2017; Ngadze et al., 2019; Różyło et al., 2019).

#### 3.1.6. Vitamins

The fruits are also a rich source of the retinol (16.11), riboflavin (0.264), niacin (0.825) and ascorbic acid (4.385). Ascorbic acid (8.21 mg/100 g), riboflavin (0.06 mg/100 g), thiamine (0.3 mg/100 g) and phenolic content (1286.-2720 mg/g) was reported in fruits are much higher than other plant part. The presence of nutritional composition, minerals, vitamins and phenolic content suggest that fruits from *Grewia* can be used as a regular dietary supplement, an alternative economic source of minerals, vitamins and natural antioxidant with less or no side effects (Osuga et al., 2006; Saleem et al., 2012; Mesaik et al., 2013).

#### 3.1.7. Modern applications: Health Benefits as a functional food

The fruits are good for heart, respiratory disorders and blood purification, several types of fevers and diarrhoea (Pita-Calvo et al., 2017).

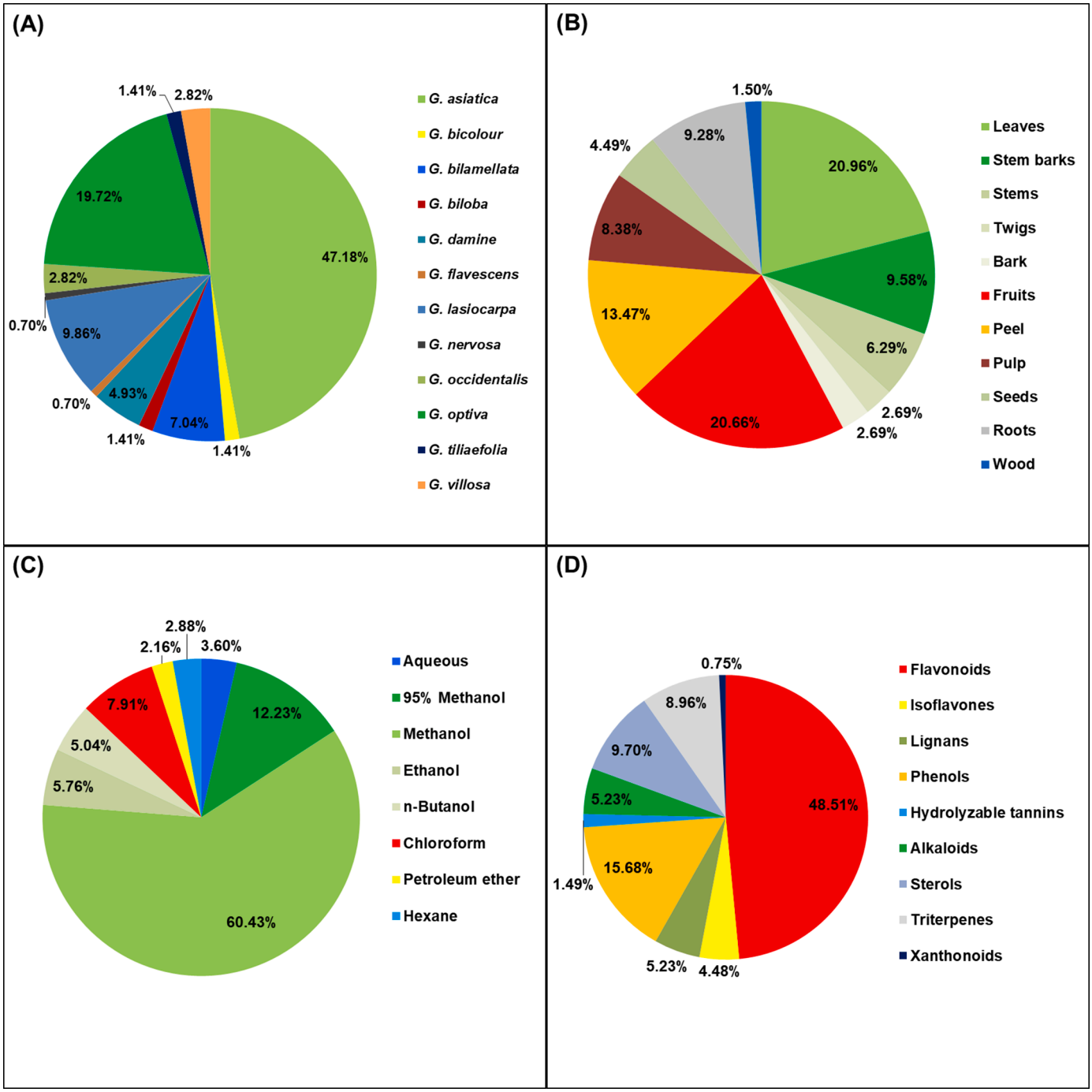


**Fig. 2.** Percentage contribution -(A) *Grewia* species, (B) plant parts, (C) various extracts and (D) classes of compounds in phytochemistry of genus *Grewia*.

According to Ayurveda, the ancient Indian treatise on medicine, the fruits are cooling tonic and aphrodisiac, they relieve thirst and burning sensation, remove biliousness, cure inflammation, heart and blood disorders and fevers (Khan et al., 2019). Moreover, fruits also contain good amounts of potent antioxidants such as flavonoids that helps in reduction of harmful free radicals produced during metabolic oxidation (Sulieman and Mariod, 2019). Due to sufficient amount of Na, it is useful in maintaining imbalanced electrolytes concentration of Na, Cl and K in bloodstream and controls the transmission of impulses (Yadav et al., 1999; Abdualrahman et al., 2011; Aboagarib et al., 2015; Hamid et al., 2016). The ripe fruits are effectively used to treat the anaemia due to immense quantities of Fe and helps in boosting haemoglobin level as well as fighting dizziness and fatigue. Due the high content of Ca fruit from *Grewia* are extremely important in curing severe pain in bones, in conditions of arthritis, osteoporosis and also helps to increase the mobility of joints. Consumption of fruits juice along with lemon and ginger essence, have wonderful beneficial effects in manifestations of the lungs irritation such as in asthma, bronchitis and cold and cough. Fruit juice is infused with water, which makes this delicious summer fruit a perfect choice, for cooling the heated up body. Fruit juice helps in relieving digestive problems like excess acidity and indigestion. The unripe fruit is more a blood purifier, normalizes heart rate, blood pressure and cholesterol levels. It relieves fevers, inflammations and blood disorders. The fruit juice helps in smooth passing of urine so it is also recommended in the cases of oliguria or low urine output disorders. It is used as a treatment of micturition (i.e a burning sensation experienced

**Table 4**
Chemical compounds and their pharmacological properties isolated from extracts of different parts of Genus *Grewia*.

| No. | Compound name | Class of compound | Plant species | Plant part | Extract | Activity | Reference |
|---|---|---|---|---|---|---|---|
| | Alkaloids | | | | | | |
| | *n*-Methyl microcosamine B | Piperidine | *G. nervosa* | Root | Methanolic | Antidiabetic (glucosidase inhibitory) | Meena et al. (2017a) |
| | Microgrewiapine A | Piperidine | *G. nervosa* | Root | Methanolic | Antidiabetic (glucosidase inhibitory) | Meena et al. (2017a) |
| | Microcosamine B | Piperidine | *G. nervosa* | Root | Methanolic | Antidiabetic (glucosidase inhibitory) | Meena et al. (2017a) |
| | Homomicrogrewiapine | Piperidine | *G. nervosa* | Root | Methanolic | Antidiabetic (glucosidase inhibitory) | Meena et al. (2017a) |
| | Harman | *β*-Carboline | *G. bicolour* | Root | Methanolic and petroleum ether | Antispasmodic and sedative | Jaspers et al. (1986) |
| | 6-Methoxyharman | *β*-Carboline | *G. bicolour* | Root | Methanolic and petroleum ether | Antispasmodic and sedative | Jaspers et al. (1986) |
| | 6-Hydroxyharman | *β*-Carboline | *G. bicolour* | Root | Methanolic and petroleum ether | Antispasmodic and sedative | Jaspers et al. (1986) |
| | Flavonoids | | | | | | |
| | Catechin | Flavan | *G. asiatica*, *G. villosa* | Fruit and stem bark | Methanolic and chloroform | Antimutagenic and antioxidant, | Geetha et al., (2004); Liu et al., (2008); Koley et al. (2020) |
| | Epicatechin | Flavan | *G. asiatica* | Fruit | 50% hydro-methanolic | Antidiabetic, Antiinflammatory, antimicrobial, antioxidant, antitumor and cardiovascular | Prakash et al., (2019); Qamar et al. (2020) |
| | 7-*O*-methylcatechin | Flavan | *G. optiva* | Root | Ethyl acetate fraction | Antioxidant | Bari et al., 2019b |
| | Epigallocatechin | Flavan | *G. asiatica* | Fruit | Methanolic | | Koley et al. (2020) |
| | (-)-Epigallocatechin-7-*O*-glucuronide | Flavan (*O*-glycoside) | *G. asiatica* | Fruit | Methanolic | | Koley et al. (2020) |
| | Vitexin | Flavone (*C*-glycoside) | *G. damine* | Leaves | Methanolic and *n*-butanol, | anticancer, antihyperalgesic, antiinflammatory, antioxidant and neuroprotective | Jayasinghe et al., 2004 |
| | Isovitexin | Flavone(*C*-glycoside) | *G. damine* | Leaves | Methanolic and *n*-butanol, | Anticancer, antiinflammatory and antioxidant | He et al. (2016); Jayasinghe et al. (2004) |
| | Apigenin-6-*C*-galactoside-8-*C*-arabinoside | Flavone (*C*-glycoside) | *G. asiatica* | Fruit | Methanolic | | Koley et al. (2020) |
| | Apigenin-7-*O*-apiosylglucoside | Flavone (*O*-glycoside) | *G. asiatica* | Fruit | Methanolic | | Koley et al. (2020) |
| | Apigenin-7-*O*-rutinoside | Flavone (*O*-glycoside) | *G. optiva* | Stem and root | 95% methanolic | | Zahoor et al. (2020) |
| | Luteolin-4'-glucoside | Flavone (*O*-glycoside) | *G. asiatica* | Fruit | Methanolic | Antiallergic, anticancer, antiinflammatory, antioxidant and hyperuricemia | Lin et al. (2018); Koley et al. (2020) |
| | Luteolin-7-*O*-(2-apiosyl-6-malonyl)-glucoside | Flavone (*O*-glycoside) | *G. asiatica* | Fruit | Methanolic | | Koley et al. (2020) |
| | 6-Hydroxyluteolin | Flavone | *G. asiatica* | Fruit | Methanolic | | Koley et al. (2020) |
| | 6-Methoxyluteolin/Nepetin | Flavone | *G. asiatica* | Fruit | Methanolic | | Koley et al. (2020) |
| | Quercetin | Flavonol | *G. asiatica* | Fruit | 50% hydromethanolic | Anti-HIV, antiinflammatory, antimicrobial, antioxidant, antitumor and antiulcer | Zheng et al., (2017); Qamar et al. (2020) |
| | 3-*O*-*β*-D-glucopyranosylquercetin | Flavonol (*O*-glycoside) | *G. damine* | Leaves | Methanolic and *n*-butanol, | | Jayasinghe et al. (2004) |
| | Quercetin-3-*O*-xyloside | Flavonol (*O*-glycoside) | *G. asiatica* | Fruit | Methanolic | | Koley et al. (2020) |
| | Quercetin-7-*O*-glucoside | Flavonol (*O*-glycoside) | *G. asiatica* | Fruit | Methanolic | Acute pancreatitis | Seo et al. (2019); Koley et al. (2020) |
| | Quercetin 3,7-di-*O*-glucoside | Flavonol (*O*-glycoside) | *G. optiva* | Stem and root | 95% Methanolic | | Zahoor et al. et al., 2020 |
| | Quercetin-7-*O*-sophoroside | Flavonol (*O*-glycoside) | *G. optiva* | Stem and root | 95% Methanolic | | Zahoor et al. et al., 2020 |
| | Quercetin-4'-*O*-glucoside | Flavonol (*O*-glycoside) | *G. asiatica* | Fruit | Methanolic | Anti-depressant | Singh et al. (2019); Koley et al. (2020) |
| | Quercetin-3-*O*-(6''-malonyl-glucoside) | Flavonol (*O*-glycoside) | *G. asiatica* | Fruit | Methanolic | | Koley et al. (2020) |
| | Quercetin-3-*O*-glucosyl-xyloside | Flavonol (*O*-glycoside) | *G. asiatica* | Fruit | Methanolic | | Koley et al. (2020) |
| | Quercetin-3-*O*-galactoside-7-*O*-rhamnoside | Flavonol (*O*-glycoside) | *G. asiatica* | Fruit | Methanolic | | Koley et al. (2020) |
| | Quercetin-3-*O*-(6''-malonyl-glucoside)-7-*O*-glucoside | Flavonol (*O*-glycoside) | *G. asiatica* | Fruit | Methanolic | | Koley et al. (2020) |
| | | | *G. optiva* | | 95% Methanolic | | Zahoor et al. (2020) |

(*continued on next page*)

**Table 4** (*continued*)

| No. | Compound name | Class of compound | Plant species | Plant part | Extract | Activity | Reference |
|---|---|---|---|---|---|---|---|
| | Quercetin-3-(caffeoyl-diglucoside)-7-glucoside | Flavonol (*O*-glycoside) | | Stem and root | | | |
| | Kaempferol | Flavonol | *G. asiatica* | Fruit | Methanolic | Antiallergic, anticancer, antidiabetic, antiinflammatory, antiobesity, antioxidant, antiplatelet and cardioprotective | Imran et al. (2019); Koley et al. (2020) |
| | Kaempferol-3-*O*-glucoside | Flavonol (*O*-glycoside) | *G. asiatica* | Fruit | Methanolic | Analgesic and antiinflammatory | Parveen et al. (2007); Koley et al. (2020) |
| | Kaempferol-3-*O*-xylosyl-glucoside | Flavonol (*O*-glycoside) | *G. asiatica* | Fruit | Methanolic | | Koley et al. (2020) |
| | 3-*O*-*β*-D-glucopyranosylkaempferol | Flavonol (*O*-glycoside) | *G. damine* | Leaves | Methanolic and *n*-butanol, | | Jayasinghe et al. (2004) |
| | 3-*O*-L-rhamnopyranosyl(1→2)-*β*-D-glucopyranosylkaempferol (kaempferol 3-O-*β*-neohesperidoside or Kaempferol-3-*O*-*β*-D-glucorhamnoside) | Flavonol (*O*-glycoside) | *G. asiatica* and *G. damine* | Fruit and leaves | Methanolic and *n*-butanol, | Anticancer and antioxidant | Akdemir et al. (2001); Youssef Moustafa et al. (2009); Koley et al. (2020) |
| | Kaempferol-3-*O*-galactoside-7-*O*-rhamnoside | Flavonol (*O*-glycoside) | *G. asiatica* | Fruit | Methanolic | | Koley et al. (2020) |
| | Kaempferol-3-(*p*-coumaroyl-diglucoside)-7-glucoside | Flavonol (*O*-glycoside) | *G. optiva* | Stem and root | 95% Methanolic | | Zahoor et al. (2020) |
| | Kaempferol 3-(caffeoyl-diglucoside)-7-rhamnosyl | Flavonol (*O*-glycoside) | *G. optiva* | Stem and root | 95% Methanolic | | Zahoor et al. (2020) |
| | Kaempferol-3-feruloylsophoroside-7-glucoside | Flavonol (*O*-glycoside) | *G. optiva* | Stem and root | 95% Methanolic | | Zahoor et al. (2020) |
| | Myricetin | Flavonol | *G. asiatica* | Fruit | 50% Hydro-methanolic | Antiamyloidogenic antibacterial, anticancer, antidiabetic, antiinflammatory, antimicrobial, antioxidant, antiplatelet antiviral and cardiovascular | Park et al. (2016); Wang et al. (2019); Qamar et al. (2020); Ha et al. (2017);Koley et al. (2020) |
| | Myricetin-3-*O*-arabinoside | Flavonol (*O*-glycoside) | *G. asiatica* | Fruit | Methanolic | | Koley et al. (2020) |
| | Myricetin-3-*O*-rhamnoside | Flavonol (*O*-glycoside) | *G. asiatica* | Fruit | Methanolic | Anticancer, antiinflammatory and antioxidant | Koley et al. (2020); Parvez et al. (2020) |
| | Myricetin-3-*O*-galactoside | Flavonol (*O*-glycoside) | *G. asiatica* | Fruit | Methanolic | Antioxidant | Hayder et al. (2008); Koley et al. (2020) |
| | Methylgalangin | Flavonol | *G. asiatica* | Fruit | Methanolic | | Koley et al. (2020) |
| | Rhamnetin | Flavonol | *G. asiatica* | Fruit | Methanolic | Anticancer, antiinflammatory antioxidant and antituberculosis | Novo Belchor et al., (2017); Koley et al. (2020) |
| | Isorhamnetin 3-glucoside-7-xyloside | Flavonol (*O*-glycoside) | *G. asiatica* | Fruit | Methanolic | | Koley et al. (2020) |
| | Morin (3, 5, 7, 2, 4-pentahydroxyflavone) | Flavonol | *G. asiatica,* and *G. optiva* | Fruit and root | Methanolic, 95% methanolic | antioxidant, chemopreventive, immunomodulatory and neuroprotective | Ben-Azu et al. (2018); Koley et al. (2020); Zahoor et al. (2020) |
| | 3′,6′,8′-trihydroxyl-4H chromen-4′-one | Flavonol | *G. optiva* | Root | 95% hydro-methanolic | Anticancer and antioxidant | Bari et al. (2019b) |
| | 7-Hydroxyflavanone | Flavanone | *G. asiatica* | Fruit | Methanolic | Antifungal, antioxidant and antitumor | Mikell et al. (2012); Koley et al. (2020) |
| | Liquiritigenin | Flavanone | *G. asiatica* | Fruit | 50% hydro-methanolic | Antidiabetic and antiinflammatory | Su et al. (2016); Qamar et al. (2020) |
| | Narirutin | Flavanone | *G. asiatica* | Fruit | Methanolic | Antiamyloidogenic and antioxidant | Chakraborty & Basu, (2017); Koley et al. (2020) |
| | Hesperetin-3'-*O*-glucuronide | Flavanone (*O*-glycoside) | *G. asiatica* | Fruit | Methanolic | | Koley et al. (2020) |
| | Dihydroquercetin | Flavanone | *G. asiatica* | Fruit | Methanolic | Antioxidant, antitumor and cardiovascular | Sunil & Xu (2019); Koley et al. (2020) |
| | Dihydroquercetin-3-*O*-hexoside | Flavanone (*O*-glycoside) | *G. asiatica* | Fruit | Methanolic | | Koley et al. (2020) |
| | Petunidin | Anthocyanin | *G. asiatica* | Fruit | Methanolic | Anticancer and antioxidant | Rajan et al., (2019); Koley et al. (2020) |
| | Cyanidin-3-*O*-arabinoside | Anthocyanin (*O*-glycoside) | *G. asiatica* | Fruit | Methanolic | Antioxidant | Hwang et al. (2014); Koley et al. (2020) |
| | Cyanidin-3-*O*-sambubioside | | *G. asiatica* | Fruit | Methanolic | Anticancer | |

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**Table 4** (*continued*)

| No. | Compound name | Class of compound | Plant species | Plant part | Extract | Activity | Reference |
|---|---|---|---|---|---|---|---|
| | | Anthocyanin (*O*-glycoside) | | | | | Lee et al. (2013); Koley et al. (2020) |
| | Cyanidin-3-*O*-(6’’-malonyl-3’’-glucosyl-glucoside) | Anthocyanin (*O*-glycoside) | *G. asiatica* | Fruit | Methanolic | | Koley et al. (2020) |
| | Cyanidin-3-*O* (6"acetyl glucoside) | Anthocyanin (*O*-glycoside) | *G. asiatica* | Ripe fruit | Methanolic | | Talpur et al. (2017) |
| | Cyanidin 3-galactoside | Anthocyanin | *G. asiatica* | Fruit | Methanolic | Antidiabetic, hepatoprotective and radioprotective | Adisakwattana et al. (2009); Ullah et al., (2012) |
| | Delphinidin-3-*O*-arabinoside | Anthocyanin (*O*-glycoside) | *G. asiatica* | Fruit | Methanolic | Antioxidant | Montoro et al. (2006); Koley et al. (2020) |
| | Delphinidin-3-*O*-sambubioside | Anthocyanin (*O*-glycoside) | *G. asiatica* | Fruit | Methanolic | Antioxidant and hypoglycaemic | Xu et al. (2017); Koley et al. (2020) |
| | Delphinidin 3-*O*-glucoside | Anthocyanin (*O*-glycoside) | *G. asiatica* | Ripe fruit | Methanolic | Antioxidant | Beninger & Hosfield (2003); Talpur et al. (2017) |
| | Peonidin 3-*O*- glucoside | Anthocyanin (*O*-glycoside) | *G. asiatica* | Ripe fruit | Methanolic | | Hidalgo et al. (2010); Talpur et al. (2017) |
| | Peonidin-3-*O* (6"-acetyl glucoside) | Anthocyanin (*O*-glycoside) | *G. asiatica* | Ripe fruit | Methanolic | | Talpur et al. (2017) |
| | Pelargonidin 3-*O*-(6’’-malonyl-glucoside) | Anthocyanin (*O*-glycoside) | *G. asiatica* | Ripe fruit | Methanolic | | Talpur et al. (2017) |
| | Pelargonidin-3-*O*-(6”acetyl glucoside) | Anthocyanin (*O*-glycoside) | *G. asiatica* | Ripe fruit | Methanolic | | Talpur et al. (2017) |
| | Malvidin-3-*O*-glucoside pyruvic acid | Anthocyanin (*O*-glycoside) | *G. asiatica* | Ripe fruit | Methanolic | | Talpur et al. (2017) |
| | Isoflavonoids | | | | | | |
| | 6-Aldehydoisoophiopogonone | Isoflavone | *G. asiatica* | Fruit | 50% Hydro-methanolic | | Qamar et al. (2020) |
| | Calycosin | Isoflavone (*O*-glycoside) | *G. asiatica* | Fruit | 50% Hydro-methanolic | antiinflammatory, antioxidant and antitumor | Li et al. (20200; Qamar et al. (2020) |
| | Dihydrodaidzein-7-*O*-glucuronide | Isoflavonone (*O*-glycoside) | *G. asiatica* | Fruit | Methanolic | | Koley et al. (2020) |
| | 6,7,3’,4’-Tetrahydroxyisoflavone | Isoflavone | *G. asiatica* | Fruit | Methanolic | | Koley et al. (2020) |
| | 5,7,8,3’,4’-Pentahydroxyisoflavone | Isoflavone | *G. asiatica* | Fruit | Methanolic | | Koley et al. (2020) |
| | Genistein | Isoflavone | *G. asiatica* | Fruit | 50% Hydro-methanolic | Antiangiogenic, antibacterial anticancer, antioxidant and oestrogenic | Qamar et al. (2020) |
| | Phenols and phenolic acids | | | | | | |
| | 8-*O*-4’-Neolignanguaia-cylglycerol-*β*-coniferyl ether (threo) | Neolignan | *G. bilamellata* | Leaves, twigs and Stem | Methanolic | Antimalarial and cytotoxicity | Ma et al. (2006); Ullah et al. (2012) |
| | 8-*O*-4’-Neolignanguaia-cylglycerol-*β*-coniferyl ether (erythro) | Neolignan | *G. bilamellata* | Leaves, twigs and Stem | Methanolic | Antimalarial and cytotoxicity | Ma et al. (2006); Ullah et al. (2012) |
| | Nitidanin | Neolignan | *G. bilamellata* | Leaves, twigs and Stem | Methanolic | Antimalarial | Ma et al. (2006) |
| | Bilagrewin | Neolignan | *G. bilamellata* | Leaves, twigs and Stem | Methanolic | Antimalarial | Ma et al. (2006) |
| | Cleomiscosin D | Coumarinolignan | *G. bilamellata* | Leaves, twigs and Stem | Methanolic | Antimalarial | Ma et al. (2006) |
| | Grewialin | Coumarinolignan | *G. optiva* | Stem bark | Ethanolic | | Uddin et al. (2013) |
| | Grewin | Coumarinolignan | *G. bilamellata* | Leaves, twigs and Stem | Methanolic | Antimalarial | Ma et al. (2006) |
| | Umbelliferone | Phenol (coumarins) | *G. asiatica* | Fruit | Methanolic | Antibacterial, anticancer, Antiinflammatory, antihyperglycaemic, antioxidant, antimicrobial and antimolluscicidal | Singh et al. (2010); Koley et al. (2020) |
| | 1,2,3 benzene triol | Phenol | *G. optiva* | Root | Ethyl acetate fraction | Antioxidant | Bari et al. (2019b) |
| | Syringaldehyde (4-hydroxy-3,5 dimethoxybenzaldehyde) | Phenol | *G. occidentalis* | Bark and wood | Aqueous | Uterotonic | Mulholland et al. (2002) |
| | 2-Methoxy-4-vinylphenol | Phenol | *G. lasiocarpa* | Leaves | Methanolic | | Akwu et al. (2019) |
| | Methyl-(2-hydroxy-3-ethoxy-benzyl)ether | Phenol | *G. lasiocarpa* | Leaves | Methanolic | | Akwu et al. (2019) |
| | 2,4-Dimethoxybenzyl alcohol | Phenol | *G. lasiocarpa* | Leaves | Methanolic | | Akwu et al. (2019) |
| | Optivanin | Phenol | *G. optiva* | Stem bark | Ethanol | | Uddin et al. (2013) |
| | Vidalenolone | Phenol | *G. asiatica* | Fruit | | | Qamar et al. (2020) |

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**Table 4** (*continued*)

| No. | Compound name | Class of compound | Plant species | Plant part | Extract | Activity | Reference |
|---|---|---|---|---|---|---|---|
| | | | | | 50% Hydro-methanolic | | |
| | 4-((1*E*)-3-Hydroxy-1-propenyl)-2-methoxyphenol | Phenol | *G. lasiocarpa* | Leaves | methanolic | | Akwu et al. (2019) |
| | Coniferaldehyde | Phenol | *G. occidentalis* | Bark and wood | Aqueous | memory boosters and uterotonic | Mulholland et al. (2002); Jeon et al. (2019) |
| | Sinapaldehyde (*E*)-4-hydroxy-3,5-dimethoxycinnam aldehyde) | Phenol | *G. occidentalis* | Bark and wood | Aqueous | Uterotonic | Mulholland et al. (2002) |
| | *p*-Coumaroyl glycolic acid | Phenolic acid | *G. asiatica* | Fruit | Methanolic | Antioxidant | Kadam et al. (2018); Koley et al. (2020) |
| | Gallic acid | Phenolic acid | *G. asiatica* | Fruit | 50% Hydro-methanolic | anti-HIV, antiinflammatory, antimicrobial and antioxidant, | Qamar et al. (2020); Li et al. (2017) |
| | Vanillic acid | Phenolic acid | *G. optiva* | Stem and root | 95% Methanolic | | Zahoor et al. (2020) |
| | Syringic acid | Phenolic acid | *G. optiva* | Stem and root | 95% Methanolic | | Zahoor et al. (2020) |
| | Caffeic acid | Hydroxycinnamic acid | *G. asiatica,* and *G. optiva* | Fruit, Stemand root | 50% Hydro-methanolic 95% and methanolic | Anticancer, antimicrobial, antioxidant and neuroprotective, | Spagnol et al. (2019); Qamar et al. (2020); Zahoor et al. (2020) |
| | Rosmarinic acid | Hydroxycinnamic acid | *G. optiva* | Stem and root | 95% Methanolic | | Zahoor et al. (2020) |
| | Salvianolic acid D | Hydroxycinnamic acid | *G. asiatica* | Fruit | Methanolic | | Koley et al. (2020) |
| | 3,5 Dihydroxy phenyl acrylic acid | Hydroxycinnamic acid | *G. optiva* | Root | Methanolic: aqueous (95:5) | Antioxidant | Bari et al. (2019b) |
| | Chlorogenic acid (5-Caffeoylquinic acid) | Hydroxycinnamic acids | *G. asiatica,* and *G. optiva* | Fruit, Stem and root | Methanolic and 50% hydro-methanolic, 95% methanolic | antimicrobial, anti-hypertension antiinflammatory, antiobesity, antioxidant, antipyretic, antiviral cardioprotective, hepatoprotective and neuroprotective, | Naveed et al. (2018); Qamar et al. (2020); Koley et al. (2020); Zahoor et al. (2020) |
| | Mangiferin | Xanthonoid | *G. asiatica* | Fruit | 50% Hydro-methanolic | Antibacterial, antidiabetic, antiinflammatory, antioxidant and antiviral | Du et al. (2018); Qamar et al. (2020) |
| | Ellagic acid | Hydrolyzable tannin | *G. asiatica,* and *G. optiva* | Fruit, Stem and root | 95% Methanolic and 50% hydro-methanolic | Anticancer, antimicrobial, antioxidant and Anti-HIV-1 | De et al. (2018); Qamar et al. (2020); Zahoor et al. (2020) |
| | Pedunculagin | Hydrolyzable tannin | *G. optiva* | Stem and root | 95% Methanolic | Antioxidant, antitumor and carbonic anhydrase inhibitor | Zahoor et al. (2020) |
| | Mandelic acid | - | *G. optiva* | Stem and root | 95% Methanolic | Antibacterial | Zahoor et al. (2020) |
| | 2,6-dimethoxy-1-acetonylquinol | Quinone | *G. bilamellata* | Leaves, twigs and Stem | Methanolic | Antimalarial | Ma et al. (2006) |
| | Volatile compounds | | | | | | |
| | Betulin | Triterpene | *G. optiva* | Stem bark | Ethanolic | Anticancer, antiinflammatory, antioxidant, antiviral (anti-HIV) and phytotoxicity | Pavlova et al. (2003); Uddin et al. (2011); Hordyjewska et al. (2019) |
| | Betulinic acid | Triterpene | *G. optiva* | Stem bark and root | Ethanolic and ethyl acetate fraction | Analgesic, antibacterial, antidiabetic, antifungal, antiinflammatory, antioxidant, antitumor, antiviral and phytotoxicity, | Uddin et al. (2011); Ríos et al. (2018); Siddiqui et al. (2019) |
| | Oleanolic acid | Triterpene | *G. optiva* | Stem bark | Ethanolic | anticancer, antiinflammatory, antimicrobial, antioxidant and phytotoxicity | Uddin et al. (2011) |
| | Ursolic acid | Triterpene | *G. optiva* | Stem bark | Ethanolic | anticancer, antiinflammatory, antimicrobial, antioxidant and phytotoxicity | Uddin et al. (2011) |
| | Oleanonic acid | Triterpene | *G. occidentalis* | Bark and wood | Aqueous | Antileishmanial, antitrypanosomal, antitumor, antiviral, hepatoprotective and uterotonic, | Funari et al., (2016); Giner-Larza et al., (2001); Mulholland et al. (2002) |
| | Ursene-3,19,28-triol | Triterpene | *G. villosa* | | Aqueous | Uterotonic | |

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**Table 4** (*continued*)

| No. | Compound name | Class of compound | Plant species | Plant part | Extract | Activity | Reference |
|---|---|---|---|---|---|---|---|
| | | | | Milled bark and wood | | | Mulholland et al. (2002) |
| | *α*-Amyrin | Triterpene | *G. asiatica, G. flavescens,* and *G. villosa* | Leaves and Fruit | Ethanolic | Antiinflammatory, antinociceptive, antioxidant, antiplatelet and hepatoprotective | Zia-Ul-Haq et al. (2013a); Cardoso et al. (2018) |
| | 3*α*,20-lupandiol | Triterpene | *G. bilamellata* | Leaves, twigs and Stem | Methanolic | Antimalarial | Ma et al. (2006) |
| | Lupeol | Triterpene | *G. bicolour, G. damine G. lasiocarpa,* and *G. tiliaefolia* | Leaves and stem bark | Methanolic, *n*-Butanol, chloroform and hexane, | Antiarthritic, antiasthma, anticancer, antidiabetic, antiinflammatory, antinociceptive, antipyretic, cardioprotective, hepatoprotective, nephroprotective, neuroprotective and ulcerogenic, | Geetha & Varalakshmi, (2001); Jayasinghe et al. (2004); Tsai et al., (2016); Akwu et al. (2019) |
| | Friedelin | Triterpene | *G. biloba, G. lasiocarpa* and *G. tiliaefolia,* | leaves and stem Bark and | Chloroform | analgesic, anticancer, antidiabetic, antidiarrhoeal, antihypertensive, antiinflammatory antipyretic and antiulcer | Jiao et al. (2007); Liu et al. (2008); Antonisamy et al. (2015); Wei et al. (2018), Akwu et al. (2019) |
| | Epi-friedelan-3-ol | Triterpene | *G. villosa* | Bark | Chloroform | | Liu et al. (2008) |
| | 2*α*,3*β*-dihydroxyolean-12-en-28-oic acid | Triterpene | *G. bilamellata* | Leaves, twigs and Stem | Methanolic | Antimalarial | Ma et al. (2006) |
| | Daucosterol | Sterol | *G. bilamellata* and *G. optiva,* | Stem bark | Ethanolic | Antiproliferative and phytotoxicity | Uddin et al. (2011); Rajavel et al. (2017); |
| | *β*-Sitosterol | Sterol | *G. bicolour, G. biloba, G. lasiocarpa* and *G. optiva,* | Root and leaves | Methanolic and ethyl acetate fraction | antidiabetic, antifibrotic, antiinflammatory, antioxidant and antiproliferative | Rajavel et al. (2017); Bari et al. (2019b); Liu et al. (2019), Akwu et al. (2019) |
| | *γ*-Sitosterol | Sterol | *G. lasiocarpa* and *G. nervosa,* | Leaf and stem bark | Methanolic, chloroform | | Uddin et al. (2011); Akwu et al. (2019) |
| | Sitosterol *β*-D-glucoside | Sterol | *G. damine* | Leaves | Methanolic and *n*-Butanol, | Antiinflammatory | Choi et al. (2012); Jayasinghe et al. (2004) |
| | Stigmasta-3,5-dien-7-one | Sterol | *G. lasiocarpa* | Leaves | Methanolic | | Akwu et al. (2019) |
| | Cholestanol | Sterol | *G. lasiocarpa* | Stem bark | Hexane | | Akwu et al. (2019) |
| | Friedelan-3-one | Sterol | *G. lasiocarpa* | Leaves | Chloroform | | Akwu et al. (2019) |
| | Lup-20(29)-en-3-ol, acetate, (3*β*) | Sterol | *G. lasiocarpa* | Leaves, stem bark | Chloroform and hexane | | Akwu et al. (2019) |
| | Stigmast-4-en-3-one | Sterol | *G. lasiocarpa* | Stem bark | Chloroform and hexane, | | Akwu et al. (2019) |
| | Stigmasterol | Sterol | *G. lasiocarpa* | Stem bark | chloroform and hexane, | | Akwu et al. (2019) |
| | Stigmasta-5,22-dien-3-ol, acetate, (3.*β*.)- | Sterol | *G. lasiocarpa* | Leaves | Chloroform | | Akwu et al. (2019) |
| | Stigmast-5-en-3-ol, oleate | Sterol | *G. lasiocarpa* | Leaves and stem bark | Methanolic and chloroform | | Akwu et al. (2019) |
| | D-Norandrostane (5.*α*.,14.*β*.) | Sterol | *G. lasiocarpa* | Leaves | Chloroform | | Akwu et al. (2019) |
| | Tridecane | Alkane | *G. pubescens* | Leaves | Hexane | | Hamid et al. (2016) |
| | Pentadecane | Alkane | *G. tenax* | Pulp | Ether | Cytotoxic | Bruno et al. (2015); Aboagarib et al. (2015) |
| | Hexadecane | Alkane | *G. lasiocarpa* and *G. pubescens,* = | Leaves and stem bark | chloroform, hexane, | | Hamid et al. (2016); Akwu et al. (2019) |
| | Heptadecane | Alkane | *G. lasiocarpa* and *G. tenax* | Seeds, pulp and stem bark | Ether, hexane | | Aboagarib et al. (2015); Akwu et al. (2019) |
| | Tridecane, 3-methyl- | Alkane | *G. tenax* | Seeds and pulp | Ether | | Aboagarib et al. (2015) |
| | 2-Methylhexacosane | Alkane | *G. lasiocarpa* | leaves and Stem bark, | Hexane | | Akwu et al. (2019) |
| | Eicosane | Alkane | *G. lasiocarpa* | Leaves and stem bark | Methanolic, chloroform and hexane, | | Akwu et al. (2019) |
| | Heneicosane | Alkane | *G. lasiocarpa* | Stem bark | Hexane | | Akwu et al. (2019) |
| | Hexatriacontane | Alkane | *G. lasiocarpa* | Stem bark | Chloroform and hexane | | Akwu et al. (2019) |
| | Octadecane, 5-methyl- | Alkane | *G. lasiocarpa* | Stem bark | Hexane | | Akwu et al. (2019) |

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**Table 4** (*continued*)

| No. | Compound name | Class of compound | Plant species | Plant part | Extract | Activity | Reference |
|---|---|---|---|---|---|---|---|
| | Pentadecane, 8-hexyl- | Alkane | *G. lasiocarpa* | Leaves | Hexane | | Akwu et al. (2019) |
| | Heptadecane, 2,6,10,15-tetramethyl- | Alkane | *G. lasiocarpa* | Leaves and stem bark | Chloroform and hexane | | Akwu et al. (2019) |
| | 9-Hexacosene | Alkene | *G. lasiocarpa* | Leaves | Methanolic | | Akwu et al. (2019) |
| | Squalene | Alkene | *G. lasiocarpa* | Leaves | Chloroform and hexane | | Akwu et al. (2019) |
| | 9-Octadecyne | Alkyne | *G. pubescens* | Leaves | Hexane | | Hamid et al. (2016) |
| | 1-Hexadecyne | Alkyne | *G. pubescens* | Leaves | Methanolic and hexane | | Hamid et al. (2016) |
| | Ethanol | Alcohol | *G. tenax* | Seeds, pulp and peel | Ether | Antimicrobial | Somchit et al. (2003); Aboagarib et al. (2015) |
| | 1-Butanol | Alcohol | *G. tenax* | Pulp and peel | Ether | | Aboagarib et al. (2015) |
| | 1-Pentanol | Alcohol | *G. tenax* | Seeds, pulp and peel | Ether | | Zhou et al. (2014); Aboagarib et al. (2015) |
| | 1-Hexanol | Alcohol | *G. tenax* | Seeds, pulp, and peel | Ether | | Aboagarib et al. (2015) |
| | 1-Octanol | Alcohol | *G. tenax* | Pulp and peel | Ether | | Aboagarib et al. (2015) |
| | 1-Nonanol | Alcohol | *G. tenax* | Seeds, pulp and peel | Ether | | Aboagarib et al. (2015) |
| | *n*-Heptadecanol-1 | Alcohol | *G. lasiocarpa* | Stem bark | Chloroform | | Akwu et al. (2019) |
| | 1-Heneicosanol | Alcohol | *G. lasiocarpa* | Leavesand Stem bark | Hexane and methanolic | | Akwu et al. (2019) |
| | *n*-Tetracosanol-1 | Alcohol | | Stem bark | Chloroform | | Akwu et al. (2019) |
| | 2-Propanol, 1-methoxy- | Alcohol | *G. tenax* | Pulp | Ether | | Aboagarib et al. (2015) |
| | 2-Butanone, 3-hydroxy- | Alcohol | *G. tenax* | Pulp | Ether | | Aboagarib et al. (2015) |
| | 1-Butanol, 3-methyl- | Alcohol | *G. tenax* | Seeds, pulp and peel | Ether | | Aboagarib et al. (2015) |
| | 2,3-Butanediol, [S-(R*,R*)]- | Alcohol | *G. tenax* | Pulp, peel and | Ether | | Aboagarib et al. (2015) |
| | D-Allose | Alcohol | *G. lasiocarpa* | Leaves | Methanolic | | Akwu et al. (2019) |
| | 2-Penten-1-ol, (*Z*)- | Alcohol | *G. tenax* | Pulp and peel | Ether | | Aboagarib et al. (2015) |
| | 1-Octen-3-ol | Alcohol | *G. tenax* | Seeds, pulp and peel | Ether | | Aboagarib et al. (2015) |
| | 2-Octadec-9-enyloxy-ethanol | Alcohol | *G. pubescens* | Leaves | Methanolic | | Hamid et al. (2016) |
| | 2,5-Heptadien-1-ol, (*Z,E*)- | Alcohol | *G. tenax* | Pulp and peel | Ether | | Aboagarib et al. (2015) |
| | 5,9-Undecadien-2-ol, 6,10-dimethyl- | Alcohol | *G. tenax* | Pulp and peel | Ether | | Aboagarib et al. (2015) |
| | Phytol (3,7,11,15-tetramethyl-2-hexadecen-1-ol) | Alcohol | *G. lasiocarpa* and *G. pubescens,* | Leaves | Methanolic, ethyl acetate, chloroform and hexane | Antianxiety, antiinflammatory, antimicrobial, antinociceptive, antioxidant, cytotoxic, apoptosis-inducing and immune modulating, | Sheeja et al. (2016); Hamid et al. (2016); Akwu et al. (2019) |
| | 2,6,10,15,19,23-hexamethyl-, (all-E)- | Alcohol | *G. lasiocarpa* | Leaves | Hexane | | Akwu et al. (2019) |
| | 1,6,10,14,18,22-Tetracosahexaen-3-ol, | Alcohol | *G. lasiocarpa* | Leaves | Hexane | | Akwu et al. (2019) |
| | *E,E,Z*-1,3,12-Nonadecatriene-5,14-diol | Alcohol | *G. lasiocarpa* | Leaves | Hexane | | Akwu et al. (2019) |
| | 3,7,11,15-Tetramethyl-2-hexadecen-1-ol | Alcohol | *G. lasiocarpa* | Leaves | Methanolic, chloroform and hexane | | Akwu et al. (2019) |
| | 2-Furanmethanol, 5-methyl- | Alcohol | *G. tenax* | Peel | Ether | | Aboagarib et al. (2015) |
| | Benzyl alcohol | Alcohol | *G. tenax* | Seeds, pulp and peel | Ether | | Aboagarib et al. (2015) |
| | Phenylethyl alcohol | Alcohol | *G. tenax* | Pulp and peel | Ether | | Aboagarib et al. (2015) |
| | 7-Hexadecyn-1-ol | Alcohol | *G. pubescens* | Leaves | Hexane | | Hamid et al. (2016) |
| | Hexanal | Aldehyde | *G. tenax* | Pulp and peel | Ether | Antifungal | Gardini et al. (1997); Aboagarib et al. (2015) |
| | Octanal | Aldehyde | *G. tenax* | Pulp and peel | Ether | Antifungal | Aboagarib et al. (2015) |
| | Nonanal | Aldehyde | *G. tenax* | Seeds, pulp and peel | Ether | Antidiarrhoeal and antifungal | Zavala-Sanchez et al. (2002); Aboagarib et al. |

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**Table 4** (*continued*)

| No. | Compound name | Class of compound | Plant species | Plant part | Extract | Activity | Reference |
|---|---|---|---|---|---|---|---|
| | | | | | | | (2015); Zhang et al. (2017) |
| | Heptanal, 2-methyl- | Aldehyde | *G. tenax* | Peel | Ether | | Aboagarib et al. (2015) |
| | 2-Butenal | Aldehyde | *G. tenax* | Pulp | Ether | | Aboagarib et al. (2015) |
| | Decanal | Aldehyde | *G. tenax* | Seeds, pulp and peel | Ether | Antimicrobial | Aboagarib et al. (2015) |
| | *E*-14-Hexadecenal | Aldehyde | *G. lasiocarpa* | Stem bark | Hexane | | Akwu et al. (2019) |
| | Benzaldehyde | Aldehyde | *G. tenax* | Peel | Ether | Antitumor and herbicidal | Aboagarib et al. (2015) |
| | Pentanone | Ketone | *G. tenax* | Peel | Ether | | Aboagarib et al. (2015) |
| | 6-Methyl-5-hepten-2-one | Ketone | *G. tenax* | Seeds, pulp and peel | Ether | Chemotaxonomic | Crewe & Blum (1971); Aboagarib et al. (2015) |
| | 5,9-Undecadien-2-one, 6,10-dimethyl-,(*E*) | Ketone | *G. tenax* | Pulp and peel | Ether | | Aboagarib et al. (2015) |
| | 2-Pentadecanone, 6,10,14-trimethyl- | Ketone | *G. lasiocarpa* | Leaves and stem bark | Chloroform and hexane | | Akwu et al. (2019) |
| | 5,9,13-Pentadecatrien-2-one, | Ketone | *G. lasiocarpa* | Leaves | Hexane | | Akwu et al. (2019) |
| | Cyclohexadiene-1,2-dione, 3,5-bis(1,1-dimethylethyl)- | Ketone | *G. lasiocarpa* | Stem bark | Hexane | | Akwu et al. (2019) |
| | (4*Z*, 12*Z*) -Cyclopentadeca-4, 12-Dienone | Ketone | *G. hirsuta* | Leaves | Methanolic | Anticancer | Abirami and Natarajan (2014) |
| | Cyclopentadecanone, 2-hydroxy | Ketone | *G. lasiocarpa* | Leaves | Methanolic | | Akwu et al. (2019) |
| | Glutaric acid | Fatty acid | *G. optiva* | Root | Methanolic: aqueous (95:5) | Antioxidant | Bari et al. (2019a) |
| | Hexanedioic acid | Fatty acid | *G. optiva* | Root | Methanolic: aqueous (95:5) | Antibacterial and antioxidant, | Choi & Jiang (2014); Bari et al. (2019b) |
| | Pentadecanoic acid | Fatty acid | *G. lasiocarpa* | Stem bark | Chloroform and hexane | | Akwu et al. (2019) |
| | Palmitic acid (*n*-Hexadecanoic acid) | Fatty acid | *G. pubescens, G. nervosa* | Leaves | Methanolic, and ethyl acetate | Antitumor, antimicrobial and antioxidant | Yanguas-Casás et al. (2018); Hamid et al. (2016), Uddin et al. (2011) |
| | Octadecanoic acid | | *G. lasiocarpa* | Leaves | Methanolic | | Akwu et al. (2019) |
| | Heneicosanoic acid | Fatty acid | *G. villosa* | Bark | Chloroform | | Liu et al. (2008) |
| | *cis*-Vaccenic acid | Fatty acid | *G. lasiocarpa* | Leaves | Methanolic | | Liu et al. (2008) |
| | 9,12,15-Octadecatrienoic acid | Fatty acid | *G. lasiocarpa* | Leaves | Hexane | | Liu et al. (2008) |
| | *α*-Linolenic acid | Ester | *G. nervosa* | Leaf | Methanolic | Antiinflammatory | Uddin et al. (2011) |
| | 13-methylpentadecanoate | Ester | *G. pubescens* | Leaves | Hexane | | Hamid et al. (2016) |
| \ | Methylhexadecanoate | Ester | *G. pubescens* | Leaves | Methanolic | | Hamid et al. (2016) |
| | Acetic acid, ethyl ester | Ester | *G. tenax* | Seeds and pulp | Ether | | Aboagarib et al. (2015) |
| | Hexadecanoic acid, ethyl ester | Ester | *G. lasiocarpa* | Leaves and stem bark | Methanolic, chloroform and hexane | | Akwu et al. (2019) |
| | Ethyl 14-methyl-hexadecanoate | Ester | *G. lasiocarpa* | Stem bark | chloroform | | Akwu et al. (2019) |
| | Hexadecanoic acid, propyl ester | Ester | *G. lasiocarpa* | Stem bark | chloroform | | Akwu et al. (2019) |
| | Propane, 2-(ethenyloxy)- | Ester | *G. tenax* | Peel | Ether | | Aboagarib et al. (2015) |
| | 2,3-dihydroxypropyl ester, (Z,Z, Z)- | Ester | *G. lasiocarpa* | Leaves | Hexane | | Akwu et al. (2019) |
| | 1,4-Benzenedicarboxylic acid, bis (2-ethylhexyl) ester | Ester | *G. lasiocarpa* | Stem bark | hexane | | Akwu et al. (2019) |
| | Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester | Ester | *G. lasiocarpa* | Leaves | methanolic | | Akwu et al. (2019) |
| | 4,8,12,16-Tetramethylheptadecan-4-olide | Ester | *G. lasiocarpa* | Leaves | Hexane | | Akwu et al. (2019) |
| | Phytol, acetate | Ester | *G. lasiocarpa* | Leaves | Methanolic, chloroform and hexane | | Akwu et al. (2019) |
| | Oleic acid, 3-hydroxypropyl ester | Ester | *G. lasiocarpa* | Leaves | methanolic | | Akwu et al. (2019) |
| | 5,6,7,7a-tetrahydro-4,4,7a-trimethyl- | Ester | *G. lasiocarpa* | Leaves | Hexane | | Akwu et al. (2019) |
| | Coumaran | Ester | *G. lasiocarpa* | Leaves | methanolic | | Akwu et al. (2019) |
| | Furan, 2-pentyl- | Ester | *G. tenax* | Seeds and pulp | Ether | | Aboagarib et al. (2015) |
| | Butyrolactone | Ester | *G. tenax* | Seeds | Ether | | Aboagarib et al. (2015) |
| | 9-Isopropyl-1-methyl-2-methylene-5-oxatricyclo[5.4.0.0 (3,8)] undecane | Ester | *G. nervosa* | Leaf | Methanolic | | Uddin et al. (2011) |

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**Table 4** (*continued*)

| No. | Compound name | Class of compound | Plant species | Plant part | Extract | Activity | Reference |
|---|---|---|---|---|---|---|---|
| | 2(4H)-Bezofuranone, 5,6,7,7αtetrahydro | Ester | *G. tenax* | Pulp and peel | Ether | | Aboagarib et al. (2015) |
| | Benzeneacetic acid, 2-tetradecyl ester | Ester | *G. tenax* | Seeds | Ether | | Aboagarib et al. (2015) |
| | Tetradecanamide | Amide | *G. lasiocarpa* | Leaves, stem and bark | Methanolic, chloroform, hexane, | | Akwu et al. (2019) |
| | 9-Octadecenamide, (Z)- | Amide | *G. lasiocarpa* | Leaves, stem and bark | Methanolic, chloroform, and hexane | | Akwu et al. (2019) |
| \ | γ-Tocopherol (Vitamin E) | | *G. lasiocarpa,* and *G. nervosa* | Leaves | Methanolic and chloroform, | Antioxidant | Uddin et al. (2011); Sahari et al. (2017); Akwu et al. (2019) |
| | Quinic acid | Polyol | *G. asiatica* | Fruit | 50% hydro-methanolic | Antiviral (HIV, HSV-1, HSV-2) | Wang et al. (2009); Yazdi et al. (2019); Qamar et al. (2020) |

while passing urine) and acidic urine which gives rise to stone formation. Various healthy drinks and candies of fruits and fruit juice have been marketed. The Raw fruit is a blood purifier, normalizes heart rate, blood pressure and cholesterol levels. It relieves fevers, inflammations and blood disorders. It has healing and medicinal properties (Bhakuni et al., 1971; Sonawane, 2019).

## 4. Phytochemistry

A large number of natural product researches have drawn great attention to genus *Grewia* in the past ten years due to its immense medicinal properties and bioactive chemical compounds and for its nutritional value. To check the contribution of each species in progressive research, therefore the percentage (%) was calculated based on the number of research papers published on particular plant parts or species along with extracts and classes of compound (Fig. 2). Based on the present investigation, the fruits (20.66%) leave (20.96%) and *G. asiatica* species (47.18%) are relatively more explored among the twelve species from the genus *Grewia*. The chemical constituents of the genus *Grewia* are abundant in alcoholic extracts, especially methanolic (60.43%) extract, and therefore could be isolated chemical compounds from alcoholic extracts. The flavonoids (48.51%) are a major class of compounds in this genus, however phenolic acids (15.68%), steroids (9.7%), terpenoids (8.96%), lignans (5.23%), alkaloids (5.23%), and isoflavones (4.48%) have been also reported appropriate amounts. Most of the flavonoids and phenolic acids have been identified and characterized by liquid chromatography-tandem mass spectrometry (LC-MS/MS) (Aadesariya, et al., 2017b; Aadesariya et al., 2019; Koley et al., 2020; Malar et al., 2017; Qamar et al., 2020). Besides terpenoids, steroids, alkanes, alkenes, alkynes, alcohols, aldehydes, ketones, organic acids, and esters were also detected and identified as volatile compounds from different extracts of genus *Grewia* by gas chromatography-mass spectrometry (GC-MS) (Aboagarib et al., 2015; Akwu et al., 2019; Hamid et al., 2016; Meena et al., 2017b). In brief, the name of compounds, their class, isolated source, and pharmacological properties is presented in Table 4.

### 4.1. Alkaloids

Piperidine (**1-4**) and *β*-carboline (**5-7**) class of alkaloids have been reported in methanolic and petroleum ether extracts of roots of of *Grewia nervosa* (Lour.) and *Grewia* bicolour Juss, respectively (Fig. 3). These alkaloids have a basic skeleton of piperidine and structurally similar to piperidine family alkaloids and having substitutions on positions N-1, C-3, and C-8'occupied by either $CH_3$ (**1, 2**, and **4**) or OH (**1** and **3**). *β*-carboline family, genus *Grewia* alkaloids showed substitution on C-6 by $OCH_3$ (**6**) and OH (**7**) (Jaspers et al., 1986; Malar et al., 2017; Meena et al., 2017a).

### 4.2. Flavonoids

Flavonoids (**8-71**) are representing the largest class of phytoconstituents including, flavan (**8-12**), flavones (**13-21**), flavonols (**22-51**), flavanones (**52-57**) and anthocyanins (**58-71**) in this genus (Fig. 3 and 4) (Jayasinghe et al., 2004; Koley et al., 2020; Talpur et al., 2017; Ullah et al., 2012; Zahoor et al., 2020). Most of the flavonoids have been reported in methanolic extracts of different plant parts of *G. asiatica, G. asiatica, Grewia* damine Gaertn, *Grewia* optiva Fibers and *G. villosa* (Aadesariya et al., 2019; Bari et al., 2019a; Bari et al., 2019b Koley et al., 2020; Qamar et al., 2020). Flavonoids *O*-glycoside are based on the flavan, flavone, flavonol and flavanone skeletons with positions C-3, C-7 and C-4' being substituted either sugar moiety or OH (**8-57**) whereas C-3, C-2' and C-5' positions occupied by either hydroxy (OH) or sugar moiety in anthocyanin skeleton (**78-71**) (Talpur et al., 2017; Qamar et al., 2020). Besides, *C*-glycoside being substituted by sugar moiety (**13-15**) on C-6 and C-8 positions in the flavone skeleton (Akdemir et al., 2001; Geetha et al., 2004; Ha et al, 2017; Jayasinghe et al., 2004; Liu et al., 2008; Park et al., 2016; Wang et al., 2019).

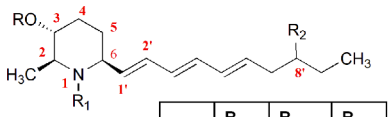
### 4.3. Isoflavonoids

Isoflavonoids (**72-77**) have been isolated from methanolic and aqueous-methanolic extracts from *G. asiatica* fruits for the first time (Qamar et al., 2020) (Fig. 5). Some of isoflavonoids (**74-76**) have been identified and characterized in methanolic extracts of *G. asiatica* fruits by LC-MS/MS. The structure of isoflavones is mainly based on isoflavone skeleton with commonly substituted either OH or sugar on positions C-7 and C-4' (**72-77**) (Koley et al., 2020; Li et al., 2017; Qamar et al., 2020).

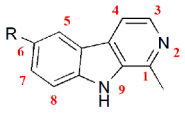
### 4.4. Phenols and others

Two new neolignans (**78-81**) have been isolated from methanolic extracts of aerial parts of *Grewia* bilamellata Gagnep for the first time (Ma et al., 2006; Ullah et al., 2012). Coumarinolignans are non-conventional lignans (**82-84**) have been also isolated from methanolic extracts of aerial parts of *G. bilamellata*. Neolignans are dimeric structures that have *β,β′*-linkage between two phenyl propane units, and have OH and methoxy ($OCH_3$) substitution on the aromatic moieties. Coumarinolignans formed by the combination of two C-6 and C-3 units are linked between coumarins and phenyl propane's through a dioxane bridge. The neolignans and coumarino-lignans were also detected in the genus *Grewia* (Ma et al., 2006; Ullah et al., 2012). Furthermore, a coumarin (**85**) has been isolated from methanolic extracts of fruits of *G. asiatica* (Fig. 5) (Koley et al., 2020; Singh et al., 2010).

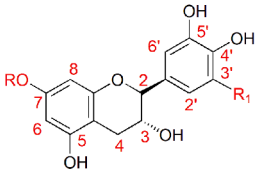
Phenols (**87-96**), phenolic acids (**97-99**), and hydroxycinnamic acids (**100-104**) have been isolated in methanolic extracts of fruits, stems and roots of *G. asiatica, G. optiva, Grewia* occidentalis L., and *Grewia*



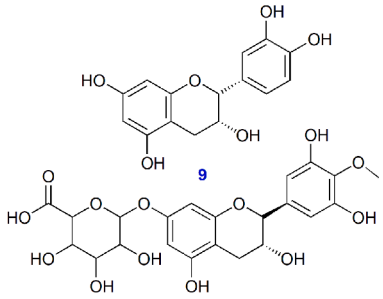
| | R | $R_1$ | $R_2$ |
|---|---|---|---|
| 1: | H | $CH_3$ | OH |
| 2: | H | $CH_3$ | H |
| 3: | H | H | OH |
| 4: | $CH_3$ | H | H |



5: R = H
6: R = $OCH_3$
7: R = OH

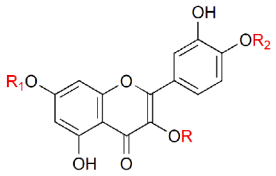


| | R | $R_1$ |
|---|---|---|
| 8: | H | H |
| 10: | $CH_3$ | H |
| 11: | H | OH |

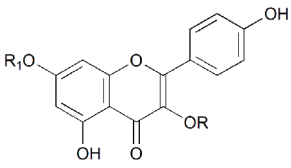


9

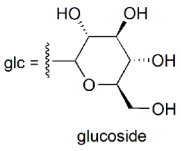
12



| | R | $R_1$ | $R_2$ |
|---|---|---|---|
| 22: | H | H | H |
| 23: | glc | H | H |
| 24: | H | xyl | H |
| 25: | H | glc | H |
| 26: | glc | glc | H |
| 27: | H | soph | H |
| 28: | H | H | glc |
| 29: | malonyl-glc | H | H |
| 30: | glc-xyl | H | H |
| 31: | glc | rha | H |
| 32: | malonyl-glc | glc | H |
| 33: | caffeoyl-diglc | glc | H |

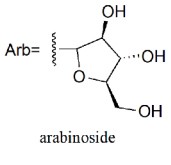


| | R | $R_1$ |
|---|---|---|
| 34: | H | H |
| 35: | glc | H |
| 36: | glc-xyl | H |
| 37: | glc | H |
| 38: | Rha-glc | H |
| 39: | gal | rha |
| 40: | *p*-coumaroyl-diglc | glc |
| 41: | caffeoyl-diglc | rha |
| 42: | Feruloy-lsoph | glc |



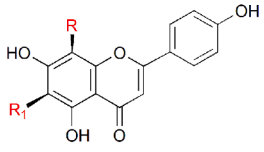
glc =

glucoside

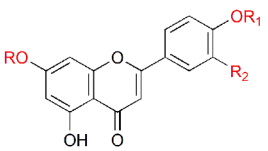


Arb=

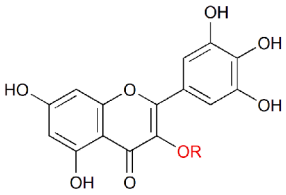
arabinoside



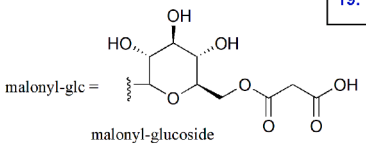
| | R | $R_1$ |
|---|---|---|
| 13: | glc | H |
| 14: | H | glc |
| 15: | glc | arb |



| | R | $R_1$ | $R_2$ |
|---|---|---|---|
| 16: | api-glc | H | H |
| 17: | rutinoside | H | H |
| 18: | H | glc | OH |
| 19: | Api-malonyl-glc | H | OH |

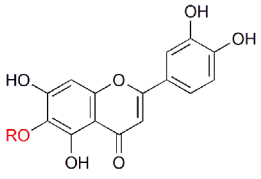


| | R |
|---|---|
| 43: | H |
| 44: | ara |
| 45: | rha |
| 46: | gal |

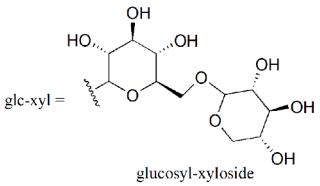


malonyl-glc =

malonyl-glucoside

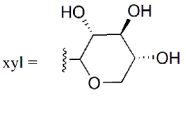


20: R = H
21: R = $CH_3$



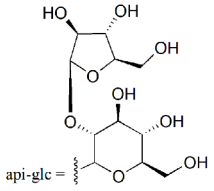
glc-xyl =

glucosyl-xyloside



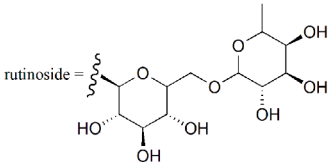
xyl =

xyloside

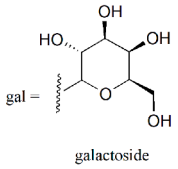


api-glc =

apiosylglucoside

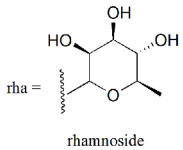


rutinoside =



gal =

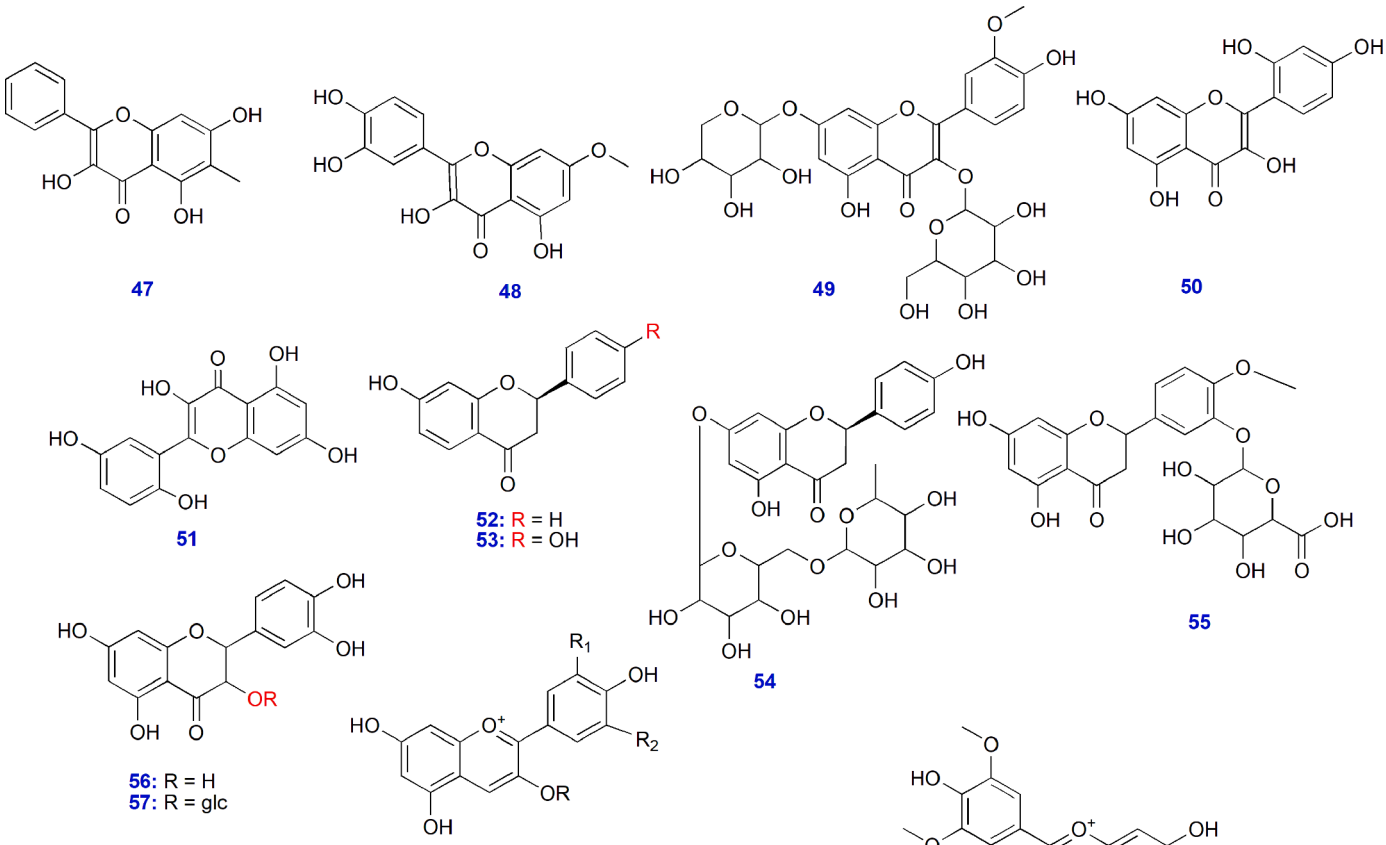
galactoside



rha =

rhamnoside

**Fig. 3.** The structure of alkaloids (**1-7**), flavans (**8-12**), flavones (**13-21**) and flavonols (**22-46**) isolated from different parts of genus *Grewia*.




| | R | $R_1$ | $R_2$ |
|---|---|---|---|
| 58: | H | OH | $OCH_3$ |
| 59: | ara | OH | H |
| 60: | sam | OH | H |
| 61: | malonyl-glc | OH | H |
| 62: | Acetyl-glc | OH | H |
| 63: | gal | OH | H |
| 64: | ara | OH | OH |
| 65: | sam | OH | OH |
| 66: | glc | OH | OH |
| 67: | glc | OH | $OCH_3$ |
| 68: | Acetyl-glc | OH | $OCH_3$ |
| 69: | malonyl-glc | H | H |
| 70: | Acetyl-glc | H | H |

**Fig. 4.** The structure of flavonols (**46-51**), flavanones (**52-57**), and anthocyanins (**58-71**) isolated from different parts of genus *Grewia*.

*lasiocarpa* E.Mey. ex Harv. Xanthonoid (**105**), hydrolysable tannins (**106-107**) aromatic alpha hydroxy acid (**108**), and quinone (**109**) have been also reported in methanolic extracts of *G. asiatica, G. optiva* and *G. bilamellata* (Fig. 5) (Ma et al., 2006; Zahoor et al., 2020).

### 4.5. Volatile compounds

Terpenoids (**110-121**), sterols (**122-134**), hydrocarbons (alkanes, alkenes, alkynes) (**135-150**), alcohols (**151-178**), aldehydes (**179-186**), ketones (**187-194**), fatty acids (**195-202**), esters (**203-223**) and amides (**224-225**) are the main volatile compounds which were identified in methanolic ethyl acetate, ether, chloroform and hexane extracts of aerial

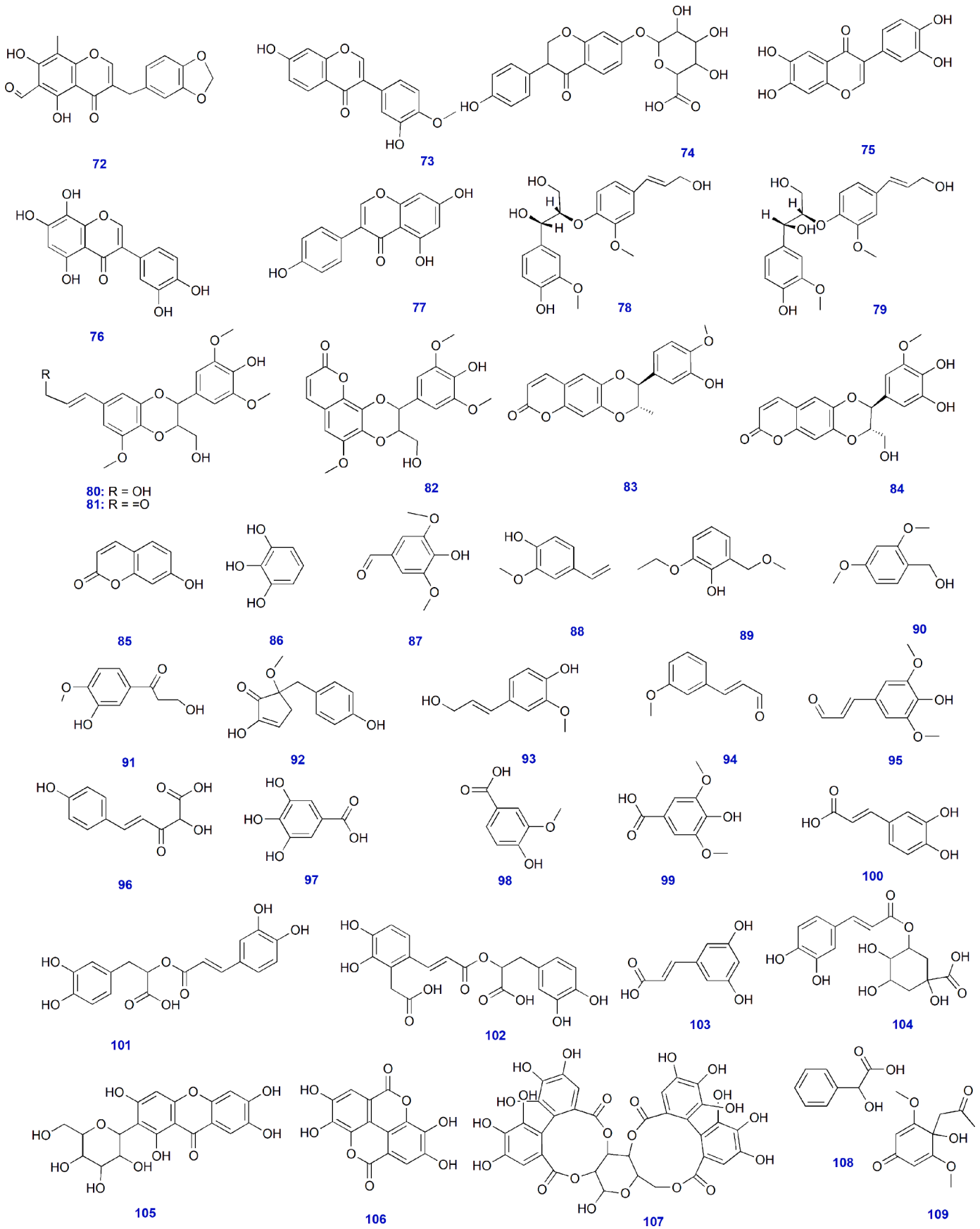



**Fig. 5.** The structure of isoflavones (**72-77**), neolignans (**78-81**), coumarinolignans (**82-84**), phenols (**85-96**), phenolic acids (**97-99**), hydroxycinnamic acids (**100-104**), xanthonoid (**105**) and hydrolyzable tannins (**106-107**) and others (**108-109**) isolated from different parts of genus *Grewia*.

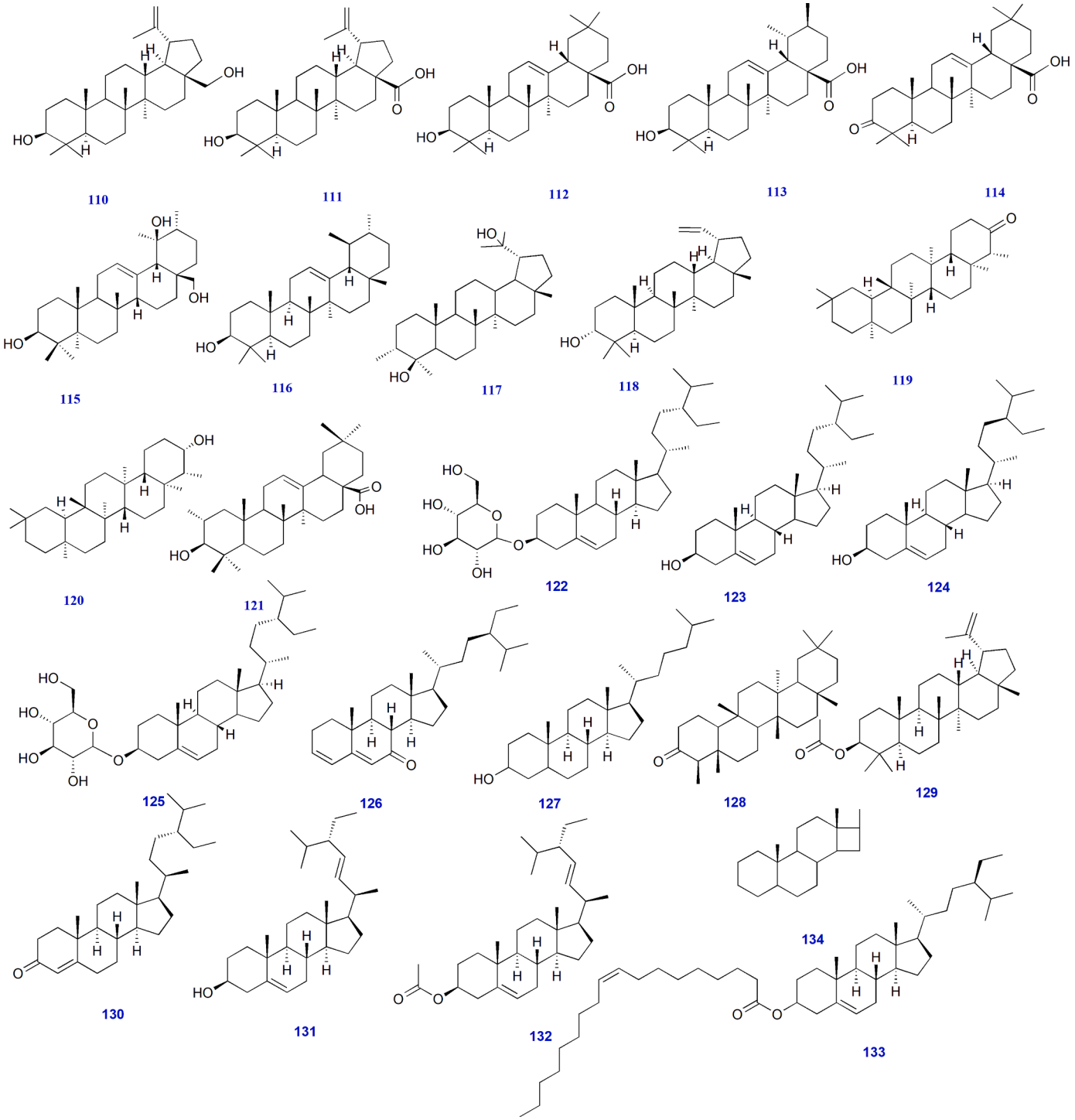



**Fig. 6.** The structure of volatile compounds, terpenes (**110-121**), steroids (**122-134**), hydrocarbons (**135-150**), alcohols (**151-178**), aldehydes (**179-186**), ketones (**187-194**), esters (**215-223**), amides (**224-225**) and others (**226-227**) isolated from different parts of genus *Grewia*.

parts of *Grewia pubescens* P.Beauv, *G. tenax, G. lasiocarpa, G. optiva, Grewia hirsute* Vahl, *G. villosa* and *G. nervosa* by GC-MS (Fig. 6). Terpenoids (**110-121**) and sterols (**122-134**) are also reported as one of the significant phytochemicals in the genus. All these terpenoids and sterols have been isolated from aqueous, ethanolic, methanolic, *n*-butanol, ethyl acetate, chloroform, and hexane fractions of *G. optiva, G. bicolour, Grewia* biloba G.Don, *G. lasiocarpa, G. bilamellata, G. tiliaefolia, G. occidentalis, G. villosa, G. flavescens*, and *G. asiatica* (Akwu et al., 2019; Antonisamy et al., 2015; Liu et al., 2008; Wei et al., 2018).23 Phytol and palmitic acid are the characteristic pharmacologically active chemical compounds from leaves of *G. pubescens, G. lasiocarpa* and *G. nervosa*. γ-Tocopherol (**226**) and quinic acid (**227**) have been also identified from leaves of *G. lasiocarpa, G. nervosa* and fruits of *G. asiatica*, respectively (Aboagarib et al., 2015; Akwu et al., 2019; Hamid et al., 2016; Sheeja et al., 2016).

## 5. Quality control

Standardization of processed or raw fruit material using analytical methods are essential to ensure the quality of raw materials and final

**Table 5**
Different analytical techniques and their methods conditions used for analysis of bioactive compounds from *Grewia spp*.

| Species | Part | Extracts | Bioactive compounds | Techniques | Mobile phase | Elusion program | Column/ plate | Flow rate ml/ min | Run time (min) | Reference |
|---|---|---|---|---|---|---|---|---|---|---|
| *G. tiliaefolia* | Rajavel | Chloroform | betulin | HPTLC | toluene-ethyl acetate, 90 + 10 (v/v) | Isocratic | TLC plates (60F-254) | | | Badami et al. (2004) |
| *G. tiliaefolia* | bark | Chloroform | lupeol | HPTLC | benzene-ethyl acetate, 95 + 5 | | TLC plates (60F-254) | | | Badami et al. (2002) |
| *G. tiliaefolia* | bark | methanol | Vitexin | HPTLC | Ethyl acetate: formic acid: water (9:1:1) | Isocratic | TLC plates (60F-254) | 1.5 | | Malar et al. (2017) |
| *G. coriacea,* | fruits | hydro ethanolic | malvidine-3-*O*-glucoside | HPTLC | Methyl acetate/ acetic acid/ formic acid/ water (80:10:10:25 v/v/v/v) | | TLC plates (Merck 60 F 254) | | | Mabika et al. (2017) |
| *G. asiatica* | Fruits | oils | *α*-tocopherol, β-tocopherol, γ-tocopherol | HPLC-DAD | *n*-heptane/ tert-butyl methyl ether (99+1, v/v) | gradient | $C_{18}$ (25 × 4.6 mm, (Merck, Darmstadt, Germany) | 1.3 | Not reported | Zia-Ul-Haq et al. (2015) |
| *G. asiatica* | Leaves | methanol (HCl, 0.1% v/v) | Delphinidin3-O- glucoside, Peonidin 3-O- glucoside, Peonidin-3-O (6"-acetyl glucoside), Cyanidin-3-O (6"acetyl glucoside), Pelarigonidin-3-O-malonyl glucoside, Pelarigonidin-3-O-(6"acetyl glucoside), Malvidin-3-O-glucoside pyruvic Acid | HPLC-DAD | methanol and formic acid solution (5% v/v) | Gradient | $C_{18}$ (250 × 4.6 mm, 5μm) | 1 | 70 | Talpur et al. (2017) |
| *G. coriacea,* | fruits | hydro ethanolic | malvidine-3-O-glucoside | HPLC-DAD | Acetonitrile and water | isocratic | $C_{18}$ (250cm 4.6 mm, 5 μm,) | 1 | | Mabika et al. (2017) |
| *G. tiliaefolia* | bark | methanol | Betulin, Lupeol, Harman, nitidanin, vitexin, isovitexin, squalene, cyclobuxine, β-amyrin, betulinic aldehyde, vitexin-4-*O*-glucoside, 3-methyl ellagic acid, ergotamine tartrate, adenine, valeric acid | LC-MS | water: methanol: THF (50:40:10) | | C-18 column | 1.5 | Not reported | Malar et al. (2017) |
| *G. asiatica* | Leaves | methanol (HCl, 0.1% v/v) | Delphinidin3-O- glucoside, Peonidin 3-O- glucoside, Peonidin-3-O (6"-acetyl glucoside), Cyanidin-3-O (6"acetyl glucoside), Pelarigonidin-3-O-malonyl glucoside, Pelarigonidin-3-O-(6"acetyl glucoside), Malvidin-3-O-glucoside pyruvic Acid | HPLC-MS | methanol and 0.1 % formic acid | Gredient | $C_{18}$ (250 × 4.6 mm, 5μm) | 1 | 49 | Talpur et al. (2017) |
| *G. tiliaefolia,* | Leaves | Petroleum ether, Benzene, Dichloromethane, Chloroform, Ethyl acetate, Acetone, Methanol and Water | β-sitosterol and Daucosterol | HPLC-MS | acetonitrile and 0.1% formic acid in water | isocratic | | | | Rajavel et al. (2017) |
| *G. tenax* | leaf | petroleum ether | | HPLC-MS | water and acetonitrile with 0.1% formic acid | Gradient | $C_{18}$ (2.0 × 150 mm, 2.5 μm) Dr Maisch, Germany | 0.6 | 16 | Aadesariya et al. (2017) |
| *G.asiatica* | fruit | 50% hydro-methanolic fraction | 16 compounds | HPLC-MS | | Gradient | direct injection | | 19 | Qamar et al. (2020) |
| *G.asiatica* | fruit pulp | methanol | 50 compounds | HPLC-MS | methanol: water with 0.1% formic acid | Gradient | BEH $C_{18}$ (2.1 × 100 mm, 1.8 μm, Waters | 0.4 | 15 | Koley et al. (2019) |

(*continued on next page*)

**Table 5** (*continued*)

| Species | Part | Extracts | Bioactive compounds | Techniques | Mobile phase | Elusion program | Column/ plate | Flow rate ml/ min | Run time (min) | Reference |
|---|---|---|---|---|---|---|---|---|---|---|
| *G. tenax* | leaves | methanol | 14 compounds | HPLC-MS | | | $C_{18}$ (2.0 × 150 mm, 2.5 µm) Dr Maisch, Germany) | 0.6 | 14 | Aadesariya et al. (2019) |
| *G. nervosa* | Root | methanol | N-Methyl microcosamine B, Microgrewiapine A, Homomicrogrewiapine, Microcosamine B | HPLC-MS | water-acetonitrile + 0.1% Formic acid | | $C_{18}$ (5 µm, 250 × 4.6 mm) | 1 | | Mabika et al. (2017) |
| *G. pubescens* | leaves | Methanol, ethyl acetate and hexane | 13 compounds | GC-MS | helium | | length; 30m x 250µm; film thickness 0.25µm) | 1 | | Hamid et al. (2016) |
| *G. tenax* | Seeds, Pulp, Peel | ether | 82 compounds | GC-MS | helium | | CP-Sil-8CB (30 m length, 0.25 mm, 0.25 µm) | 0.9 | | Aboagarib et al. (2015) |
| *G. lasiocarpa* | Leaves and stem bark | Hexane, chloroform, methanol | | GC-MS | helium | | 30 m × 0.25 mm, 0.25µm | 1.2 | | Akwu et al. (2019) |

products (Pita-Calvo et al., 2017; Luykx and Van Ruth, 2008). Currently, HPLC and LC-MS methods have played an important role in quality control of herbal and nutraceutical products. Therefore, The HPLC and LC-MS have been used to analyse wide range of diverse types of metabolites. Dangerous chemicals such as aflatoxins, pesticides, harmful chemicals and antibiotic can be detected easily by LC-MS methods even they are present in trace amount (Eissa et al., 2014; Fan et al., 2015). The different methods used for the analysis of bioactive compounds from *Grewia* species are summarized in Table 5. The molecular mass (m/z), molecular formula, identity of molecule and their distribution in different plant parts and corresponding extracts are presented in Table S1 and S2 (Supplementary data).

### 5.1. High performance high-performance thin-layer chromatography (HPTLC)

Previously proposed HPTLC methods have been used for qualitative and quantitative analysis of micronutrients and bioactive compounds such as lupeol and betulin in chloroform extracts of bark of *G. tiliaefolia*. Pre-coated plates silica gel 60 F254 has been used as stationary phase, and toluene-ethyl acetate (90:10, v/v) used as a mobile phases for separation of betulin. Lupeol has been separated using benzene-ethyl acetate (95:5, v/v) as mobile phase. The calibration curves showed the linear in the range for both compounds in the range from 0.5-1.8 µg with correlation coefficient 0.999 (Badami et al., 2002; Badami et al., 2004). Vitexin an important bioactive compounds has been also separated and quantified in methanol extract using ethyl acetate: formic acid: water (9:1:1) as mobile phase. The significant content (4.04 mg/g) of vitexin reported in the methanol extract leaves of *G. tiliaefolia* (Malar et al., 2017). Preparative TLC method has been developed for separation and quantitation of malvidine-3-*O*-glucoside from hydroethanolic extract of fruits from *G. coriacea* plant using a mixture of solvents viz ethyl acetate/acetic acid/formic acid/water (80:10:10:25 v/v/v/v) as a mobile phase. The UV lamp with 254 nm used to determine compounds (Mabika et al., 2017). The sensitivity and resolution of HPTLC showed good but are not comparable with HPLC and LC–MS methods therefor it is still a good but less prefer choice in the routine test for quality control.

### 5.2. High performance high-performance liquid chromatography

The reversed-phase $C_{18}$ columns are used with length ranging from 25-250 mm with 3.5 to 4.6 mm internal diameter along with 3-5 µm particles size. Elution programs were adopted usually binary or ternary system using different combination of methyl acetate, acetic acid, formic acid and water with the flow rate ranging from 1.0-1.3 mL/min. Maximum run times (min) was reported 70 minutes with equilibration between the 5 min. Recently, relatively improved HPLC methods have been claimed for simultaneous qualitative and quantitative analysis bioactive compounds from *Grewia* species due to its comparative high separation and detection capabilities than HPTLC. Zia-Ul-Haq et al., (2015) have been separated three isomers of tocopherols ($\alpha$-, $\beta$-, $\gamma$-) from n-heptane extracts of fruits of *G. asiatica* using combination of n-heptane/tert-butyl methyl ether (99+1, v/v) as a mobile phase. The identification and separation of tocopherols is a tedious job however the tocopherols were easily detected from ranged at 280-330 nm using developed method. Among them α-tocopherol (651:35±4:08) was detected highest amount followed by $\beta$-tocopherol (5:01±0:33) and γ-tocopherol (1:08±0:17). Results showed that the fruits have the highest nutritional importance due to isomers of tocopherols. Fruit of *G. asiatica* are a great source of anthocyanins (Zia-Ul-Haq et al., 2015). Eight anthocyanins have been separated and simultaneous quantified in acidified methanol fruits of *G. asiatica* because of this extract have high content of anthocyanins than others (water, methanol, ethanol and their binary mixture). This method is relatively long run time (70 min) with peaks tailing. Anthocyanins were detected at 265-275 (band II) and 465-560 (band I) nm in UV spectra due to restriction of conjugation between the A- and B-rings. Among them cyanidin-3-*O*-(6"acetylglucoside) reported as a major anthocyanin comprising 44-63% (695 µg/g) of total anthocyanins composition followed by peonidin-3-*O*-glucoside (3-30%; 163.6 µg/g) and pelargonidin-3-*O*-(6"-acetyl glucoside) (8-14%; 140.4µg/g). Fruit of *G. asiatica* has a significant rich source of anthocyanins (Talpur et al., 2017). $\beta$–sitosterol and daucosterol have been also separated and purified by HPLC method (Rajavel et al., 2017). Mabika et al. (2017) have reported preparative HPLC using Diode Array Detector (DAD) for quantitative analysis of malvidine-3-*O*-glucoside from hydroalcoholic extract from fruits of *G. coriacea* (Mabika et al., 2017). Often the root are not considered the best part for nutraceutical demand however the root of *G. optiva* is deliberately a good source of

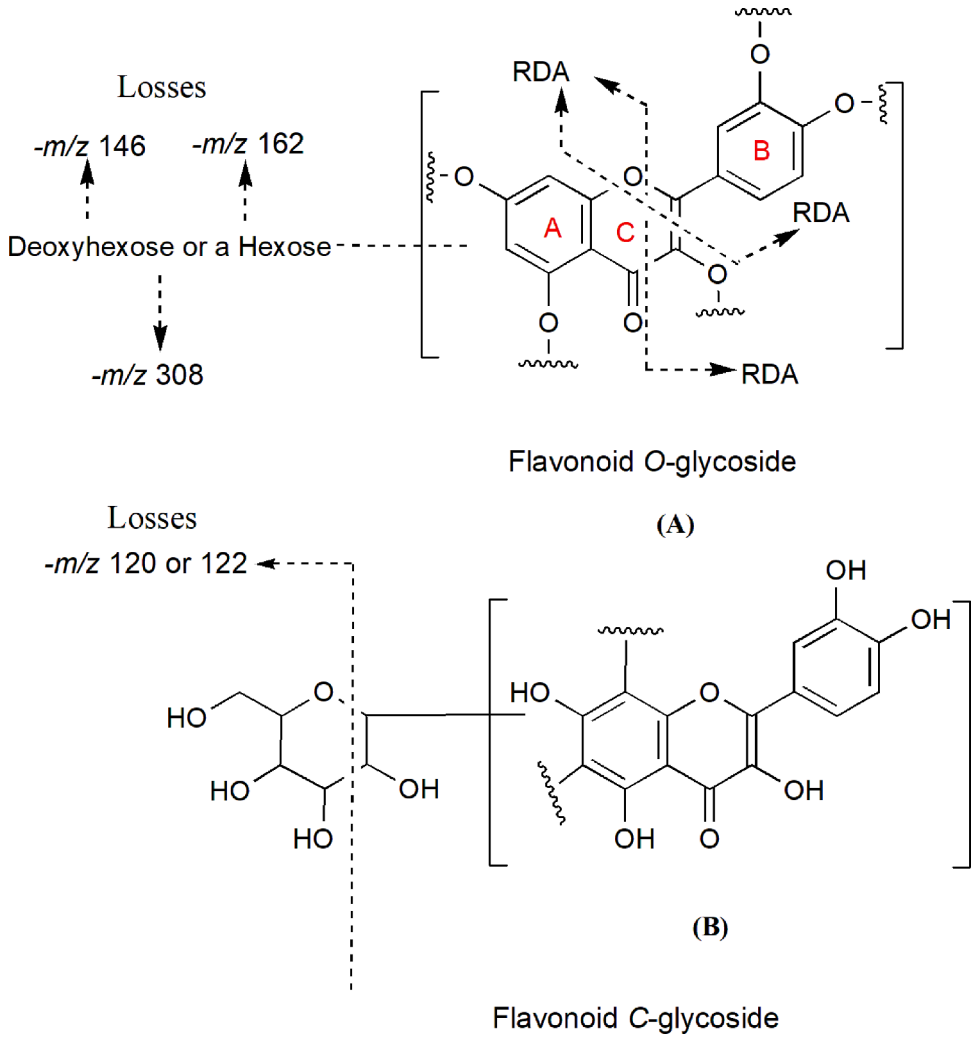



**Fig. 7.** Fragmention pathways of *O*- and *C*-flavonoids.

nutraceuical. Nineteen compounds were separated and determined in the crude extract and fractions of root of *G. optiva* by relatively more improved HPLC method using combination of methanol: acetic acid: deionized water (10:2:88, v/v) (solvent A) and methanol: acetic acid: deionized water (90:2:8, v/v) (solvent B) as a mobile phase. Highest content of ellagic acid (peak area %: 23.6949) followed by quercetin 3, 7-di-*O*-glucoside (peak area %: 7.0419), kaempferol-3-(p-coumaroyl -diglucoside)-7-glucoside (peak area %: 5.1094) and morin (peak area %: 4.8446) have been reported and relatively quantified on the basis of peak area percentage. Approximate same quantity (peak area %: 2) of syringic acid, chlorogenic acid, apigenin-7-*O*-rutinoside, quercetin-7-*O*-sophoroside, kaempferol 3-(caffeoyl-diglucoside)-7-rhamnosyl, kaempferol-3-(p-coumaroyl-diglucoside)-7-glucoside, caffeic acid, kaempferol-3-(p-coumaroyl-diglucoside)-7-glucoside were also observed (Zahoor et al. 2020). HPLC-DAD is still commonly applied for routine qualitative analysis of nutraceuticals in complex matrix. Because of the complexities of plant extracts, the simultaneous separation of most flavonoids always needed a long analysis time.

### 5.3. *High-performance chromatography-mass spectrometry*

During methods development, reversed-phase C18 columns were almost exclusively used with length ranging from 30-250 mm with 2.0-4.6 mm internal diameter along with 1.8-5 μm particles size. Chiral stationary phase (CSP) columns were not reported for analysis of nutraceutical although stereoisomers of compounds have reported in some of the recent literature. Elution programs were adopted usually with binary system using more polar solvent like water with 0.1% formic acid (solvent A), and a less polar organic solvent such as either methanol or acetonitrile (solvent B) with the flow rate ranging from 0.3-1.5 mL/min. Run times (min) are generally 15 minutes to 30 minutes, with equilibration timing in between the 3-5 min. Generally, column temperature thermostatically controlled at 25-35ºC (Aadesariya et al., 2019; Aadesariya et al., 2017; Koley et al., 2020; Qamar et al., 2020).

The past decade, several LC-MS and LC-MS/MS methods have been reported for identification of known and unknown compounds with the emphasis on distinguishing isomeric compounds in complex plant extracts with recent important developments of identification and characterization. All of these compounds identified and characterized thoroughly discussed in respect to the presence/absence of the relative abundance of distinctive fragment ions, which can help to identify and characterize important structural characteristics. Identification of the compounds from *Grewia* species have been reported either positive or negative ionization mode or in both at a same time (Malar et al., 2017; Talpur et al., 2017; Rajavel et al., 2017). Therefore previously published LC-MS methods recommended negative ionization for flavonoids and positive ionization for anthocyanins and alkaloids identification and characterization.

#### 5.3.1. *Alkaloids*

Meena et al (2017a) were detected six alkaloids (1-6) as [M+H]+ in methanol of *G. nervosa*. Their structures were elucidated using

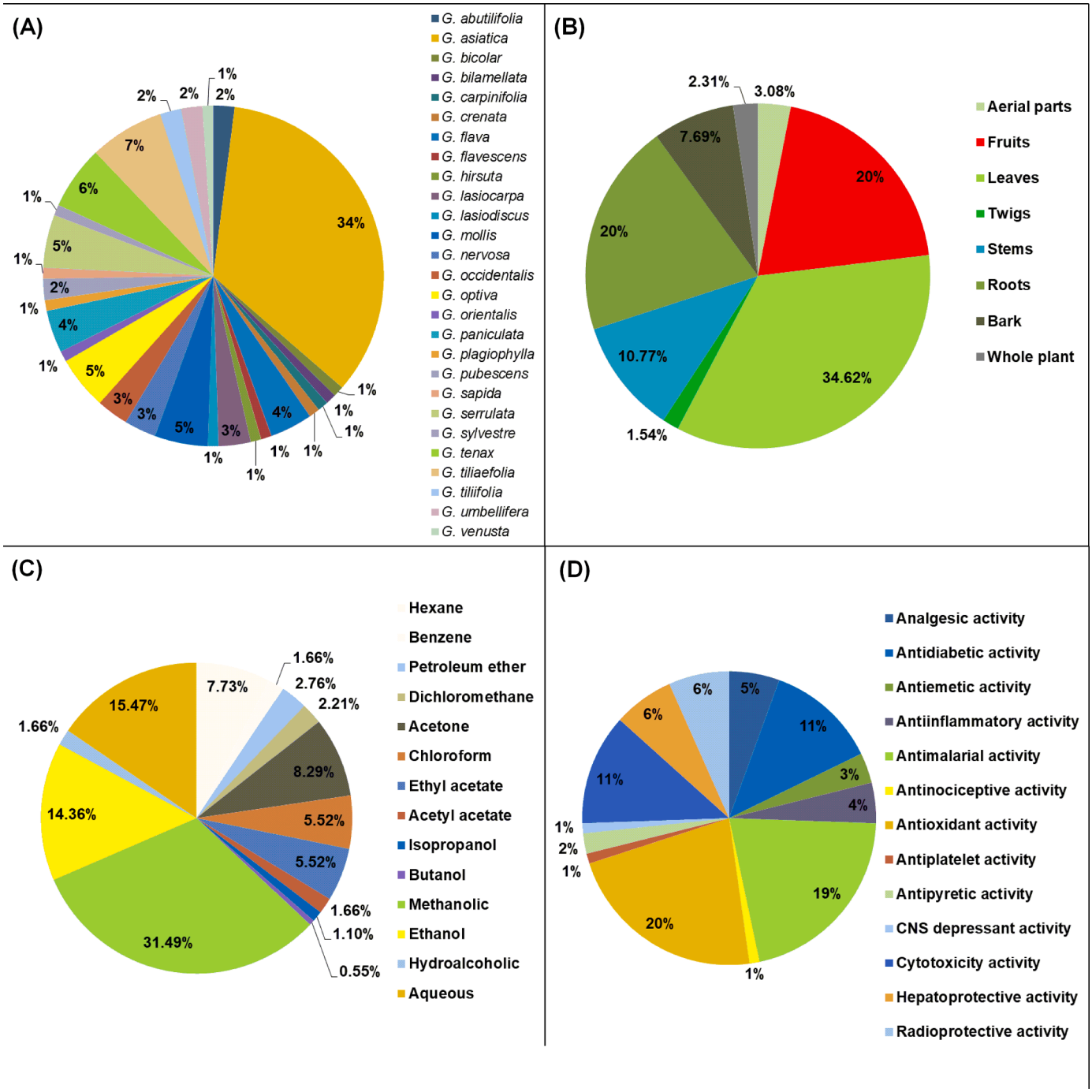



**Fig. 8.** Percentage contribution- (A) *Grewia* species, (B) Plant parts, (C) Various extracts (D) pharmacological activities of *Grewia* species.

combination of LC/HR-MS, 1H-NMR, and IR spectral analyses and followed by comparison with those reported in the literature. The problematic separation of these alkaloids on traditional column chromatography (Silica gel, Octadecyl silane, Sephadex) was resolved by using HPLC (Meena et al., 2017a).

### 5.3.2. *Flavonoids*

Seventy flavonoids were identified in alcoholic extracts from many plants of *Grewia* species on the basis of chromatographic and mass spectrometric data (Zia-Ul-Haq et al., 2012; Malar et al., 2017; Talpur et al., 2017; Rajavel et al., 2017; Aadesariya et al., 2019; Koley et al., 2020; Qamar et al., 2020; Zahoor et al., 2020; Aadesariya et al., 2017b;). The *retro*-Diels–Alder reaction (RDA) fragment ions were observed as a characteristic fragments in flavonoids especially in aglycone moiety such as quercetin (m/z 303) and kaempferol (m/z 287). Flavonoid *O*-glycoside and *C*-glycoside have distinctive fragmentation pattern. According to literature survey flavonoid *O*-glycoside yielded common losses at m/z 146 Da, m/z 162, and m/z 308 Da in MS/MS spectrum which indicates that the glycoside have a deoxyhexose and a hexose moiety. Similarly, characteristic fragment ions were produced by the losses of m/z 120 and 122 Da units in MS/MS spectrum a C-glycoside indicate the presence of a hexose and a deoxyhexose unit, respectively (Fig. 7). Many papers have been published for characterization of *O*- and C- flavonoids glycosides having mono, di and polyglycosides (Caristi et al., 2003; Singh and Singh, 2015).

Fourteen anthocyanins were identified and characterized in 1%

acidified methanolic and methanol extracts of *G. asiatica* by LC-MS/MS. All anthocyanins showed molecular ion as a [M]+. All anthocyanins were detected as glycosides except petunidin. Characteristic and abundant fragment ions were observed at m/z 271, 287, 301, 303 and 331 for pelargonidin, cyanidin, malvidin, delphinidin and malvidin, respectively due to losses of corresponding sugar moiety (Sun and Miller, 2003; Shen, et al., 2006; Jaiswal et al., 2012; Talpur et al., 2017; Koley et al., 2020;).

Five flavans (7-hydroxyflavan, catechin, epicatechin, epigallocatechin, (-)-epigallocatechin 7-*O*-glucuronide) have been reported in fruits of *G. asiatica*. 7-hydroxyflavan, catechin, epicatechin, epigallocatechin showed base peak at m/z 227, 139, 137 and 153 in positive ionization (Talpur et al., 2017; Koley et al., 2020). (-)-Epigallocatechin 7-*O*-glucuronide showed characteristic fragment ion at m/z 321 due to loss of sugar moiety in positive ionization. Most of the mass spectrometric analysis of catechin and epicatechin showed characteristic fragment ions at m/z 245, 205, 203 and 227 in MS/MS analysis with the difference observed only in relative abundance of fragment in negative ionization (Sun and Miller, 2003; Shen et al., 2006). Similarly, epigallocatechin showed characteristic fragments at 179, 261, 221, 219, 165 and 125 in negative ionization (Jaiswal et al., 2012; Umehara et al., 2017).

Seven flavanones namely liquiritigenin, dihydroquercetin (isomer), dihydroquercetin (isomer), dihydroquercetin (isomer), dihydroquercetin 3-*O*-hexoside, hesperetin 3'-*O*-glucuronide, narirutin, including three isomeric dihydroquercetin have been identified in 1% FA in methanol extract of *G. asiatica* fruits. The isomers of dihydroquercetin showed RDA as characteristic fragment ion at 153 and 137. Dihydroquercetin 3-*O*-hexoside, hesperetin 3'-*O*-glucuronide and narirutin showed corresponding fragment ions due to losses of sugar moieties (Zia-Ul-Haq et al., 2013; Zia-Ul-Haq et al., 2015; Malar et al., 2017; Talpur et al., 2017; Rajavel et al., 2017; Aadesariya et al., 2019; Koley et al., 2020; Qamar et al., 2020; Zahoor et al., 2020; Aadesariya et al., 2017b).

The flavones have been reported characteristic RDA fragment ions. *O*-glycoside of luteolin and apigenin showed characteristic fragment ions at m/z 271 and 287 due to losses of corresponding sugar moieties (162 Da) whereas *C*- glycosides gave common losses at m/z 120 Da due to hexose sugar moiety (Singh et al., 2015).

The flavonols were detected in hydro-methanolic extracts of fruits of *G. asiatica*. *O*-glycosides of kaempferol, quercetin and myricetin showed characteristic fragment ions at m/z at 287, 303 and 319. All the aglycone such as kaempferol, quercetin and myricetin showed RDA cleavage and yielded corresponding fragment ions (Qamar et al., 2020; Malar et al., 2017).

#### 5.3.8. *Isoflavonoids*

Four isoflavonoids (genistein, calycosin, 6-aldehydo-isoophiopogonone, dihydrodaidzein 7-*O*- glucuronide) were detected in fruits of *G. asiatica*. genistein, calycosin, 6-aldehydo-isoophiopogonone were produced RDA fragment ions and dihydrodaidzein 7-*O*- glucuronide showed common loss of sugar moiety (162 Da) (Zia-Ul-Haq et al., 2012a; Malar et al., 2017; Talpur et al., 2017; Rajavel et al., 2017; Aadesariya et al., 2019; Koley et al., 2020; Qamar et al., 2020; Zahoor et al., 2020; Aadesariya et al., 2017b).

#### 5.3.9. *Hydroxybenzoic and hydroxycinnamic acids*

Six phenolic acids (gallic acid (two isomers), caffeic acid, p-coumaroyl glycolic acid, chlorogenic acid, 5-caffeoylquinic acid, salvianolic acid D) were detected methanolic and hydromethanolic extracts of fruits of *G. asiatica* and showed common neutral losses of CO, CO2 and H2O and produced corresponding fragment ions. Three isomeric of gallic acid were also detected by Qamar et al., (2020).

### 5.4. *Gas chromatography-mass spectrometry*

The GC–MS analysis of the extracts from the leaves, stem bark and fruits of plants from genus *Grewia* showed the presence of a number of bioactive compounds. The identified compounds with their molecular weight, molecular formula, peak height (%) in different extracts are presented in Table S2 (Supplementary data).

Silica capillary chromatographic column with length 30 m and 0.25 μm film thickness with temperature varied from 50-250 °C. The flow rate maintained ranged from 0.9-1.2 mL/min. The GC–MS analysis of the crude extracts (hexane, chloroform, ethyl acetate and methanol) from the fruit leaves and stem bark of *G. pubescens, G. lasiocarpa, G. tenax* and *G. nervosa* revealed the presence of different classes of bioactive compounds such alcohols (28.39%), acids (27.78%), alkanes (14.28%) aldehydes (6.95%), terpens and steroids (16.01%), esters (6.59%). Content of palmitic acid (approximately 61.59%) was detected as a highest volatile compound in methanolic, ethyl acetate, and hexane extracts of leaves of *G. pubescens* among plant parts and other *Grewia* species. 3,7,11,15-tetramethyl-2- hexadecen-1-ol (approx. 29.8%) was second most abundant compound among studied species. High content of lupeol was detected in chloroform extract of stem bark of *G. lasiocarpa* followed by lup-20(29)-en-3-ol, acetate, (3.beta.) (12.87%), in methanolic extracts. Fruit of *G. tenax* showed high content of 5,9-undecadien-2-ol, 6,10-dimethyl- (11.60%) followed by nonanal (10.35%). Comparative analysis of plant parts showed leaves (63.02%) have high total content of volatile compounds followed by stem bark and (24.72%) and fruit (12.26%) (Aboagarib et al., 2015; Akwu et al., 2019).

## 5. Pharmacological activities

All studied species of *Grewia* are reported for many pharmacological activities. The contribution of various extracts of different plant parts of *Grewia* species was calculated and represented in percentage (%) (Fig. 8). The present investigation showed that *G. asiatica* (34%) is more explored species among them. Most of the pharmacological researchers are interested in alcoholic (45.85%) and aqueous (15.47%) extracts of leaves (34.62%) and fruits (20%) of plants of genus *Grewia* due to the high content of bioactive compounds. Acetone, hexane, ethyl acetate, chloroform, and dichloromethane (DCM) extracts have been also used for the investigation of biological activities. Antioxidant (20%), antimicrobial (17%), antidiabetic (11%), cytotoxicity/ anticancer (11%), hepatoprotective (6%) and radioprotective (6%) are the most considerable pharmacological activities. Analgesic, antipyretic, antiemetic, antiinflammatoryanti-inflammatory, antiplatelet, neuroprotective and nephroprotective activities have been reported in various extracts of *Grewia*. The pharmacological activities of various extracts of different plant parts of *Grewia* and its secondary metabolites are discussed and summarized in Tables 2 and 3.

### 5.1. *Analgesic activity*

The ethanolic extract and its petroleum ether, chloroform, and ethanolic fractions of the leaf of *Grewia paniculata* Roxb. ex DC.showed significant analgesic effect at a dose of 250 and 500 mg/kg (Ali et al., 2015). Similarly, methanolic extract of root bark of *G. asiatica* showed significant inhibition at 400 mg/kg (Paviaya et al., 2013). Methanolic and aqueous extracts of *G. asiatica* fruits showed significant analgesic activity at 500 mg/kg (Akhtar et al., 2016). The aqueous extract of leaves of *G. tiliaefolia* has also possessed comparable significantly analgesic activity at 250 and 500 mg/kg (Sakat & Juvekar, 2009). The hexane, chloroform, ethyl acetate and butanol extracts of leaves of *Grewia crenata* (G.Forst.) Schinz & Guillaumin are known for this activity whereas the effect of the ethyl acetate fraction (200 mg/kg) was comparable significantly (Ukwuani et al., 2014). Compounds **35, 111** and **119** showed analgesic while antinociceptive activity was observed in **116, 118** and **170** compounds (Wei et al., 2018; Cardoso et al., 2018).

### 5.2. Anticancer activity

The ethanolic extracts of *G. paniculata* leaves and bark showed moderate cytotoxic activity in brine shrimp nauplii test with $LC_{50}$ values of 3.01 µg/mL compared with vincristine (0.52 µg/mL) (Nasrin et al., 2015). The water extract of root bark of *Grewia* mollis Juss. showed the most active with $LC_{50}$ of 3.50 µg/mL, followed by the methanolic extract ($LC_{50}$ = 11.61 µg/mL) whereas acetone ($LC_{50}$ =120.77 µg/mL) and ethyl acetate ($LC_{50}$ =426.20 µg/mL) was found moderate and the least activity observed hexane ($LC_{50}$ =730.76 µg/mL,) by the brine shrimp lethality test (Mshelia et al., 2016). The methanolic extract of *G. asiatica* showed considerable 50% *in-vitro* cytotoxicity on HL– 60, K-562, MCF-7 and Hela cells at concentrations of 53.70 µg/mL, 54.90 µg/mL, 199.5 µg/mL and 177.8 µg/mL, respectively (Kakoti et al., 2011). The methanolic extract of the whole plant of *G. tiliaefolia* has possessed very good cytotoxicity on Vero and HEp-2 cell lines with their inhibit cell growth by 50% (CT $C_{50}$) values of 205 ± 13.23 and 345 ± 12.65 µg/mL, respectively (Ramshankar et al., 2008). The methanolic extract of *G. nervosa* leaf showed a significant antiproliferative and cytotoxic effect on MCF-7 breast cancer cell line (Meena et al., 2017b) whereas 95% methanolic extracts of *G. optiva* stems and roots were found to be nontoxic (Zahoor et al., 2020). The acetone extract of *G. flava* leaves, bark, and roots showed the highest $LC_{50}$ (lowest toxicity) of 551.68 68 µg/mL toward Vero cells than methanolic, acetyl acetate and water extracts of leaves, bark, and roots (Lamola et al., 2017). The 50% hydro-methanolic extracts of *G. asiatica* fruits showed maximum cytotoxic activity against MCF-7 ($IC_{50}$ 34.9 ug/mL), HEp-2 ($IC_{50}$ 80.4 ug/mL) and NCI-H522 ($IC_{50}$ 73 ug/mL) on cancer cell lines than hexane, DCM and methanolic extracts (Qamar et al., 2020). The aqueous leaf and fruit extracts of *G. asiatica* showed *in-vitro* cytotoxic activity against epidermal kidney, cell lung, cervical, laryngeal, and breast cancer cell lines. The aqueous extract of fruits was found to be active on lung cancer cell line with $IC_{50}$ of 59.03 and 58.65µg/mL in MCF-7 cell line whereas aqueous leaf extract of *G. asiatica* was found to be active on breast cancer cell line with $IC_{50}$ of 50.37µg/mL and 61.23µg/mL in Hep-2 cell lines. (Marya et al., 2011). Flavonoids (**9, 13, 14, 18, 22, 34, 38, 43, 46-46, 48, 50, 51, 52, 54, 56** and **60**), isoflavonoids (**74** and **77**), neolignans (**78** and **79**) phenol (**85**), hydrolyzable tannins (**106-107**) and volatile compounds (**110-114, 118-119, 186, 193** and **198**) showed anticancer/antitumor activity on different cell lines with different concentrations (Bruno et al.,2015; Imran et al., 2019; Novo Belchor et al., 2017; Parvez et al., 2020; Rajavel et al., 2017; Tsai et al., 2016; Zheng et al., 2017).

### 5.3. Antidiabetic activity

Antidiabetic activity of ethanolic extracts of aerial parts of *Grewia serrulata* DC., *G. asiatica* and *G. flavescens* has been reported using doses from 100-500 mg/kg and significant response found at 200 and 400 mg/kg in streptozotocin (STZ) induced hyperglycemic rats (Chandiran et al., 2013a; Chandiran et al., 2013b, Chandiran et al., 2014; Khattab et al., 2015; Khatune et al., 2016; Yanadaiah, 2013). Similarly, methanolic extracts of aerial parts of *G. asiatica* and *G. tiliaefolia* showed significant effects at doses between 200-400 mg/kg by reduction of glucose levels in normal rats (Zia-Ul-Haq et al., 2012b; Kumar et al., 2012).105 The methanolic extracts of stems and roots of *G. optiva* showed good antidiabetic properties within range of doses 200 - 500 mg/kg in induced diabetic rats (Zahoor et al., 2020).27 Crude extracts of bark of *Grewia* herbacium Vent. ex Juss., *G. asiatica* and *G. sylvestre* have been also reported for a significant reduction of cholesterol and triglycerides at 5 g/Kg dose in diabetic mice (Dogar et al., 1988). Alkaloids (**1-4**), flavonoids (**9, 34, 53** and **63**), terpenoids (**105, 111** and **118-119**) and sterol (**123**) also showed antidiabetic activity (Jaspers et al., 1986; Malar et al., 2017; Meena et al., 2017a).

### 5.4. Antiemetic activity

The methanolic, ethanolic and 70% aqueous extracts of leaves, fruits and roots of *G. asiatica* and *Grewia lasiodiscus* K.Schum.showed significant effects at doses 100 and 200 mg/kg in mice and rats. These activities of different extracts of plant parts of *G. asiatica* and *G. lasiodiscus* were comparable with antiemetic drugs such as Maxolon (Metoclopramide) and Largactil tablets 10 mg (Chlorpromazine) (Yaqeen et al., 2008; Tijani et al., 2008; Zia-Ul-Haq et al., 2012b).

### 5.5. AntiinflammatoryAnti-inflammatory activity

The methanolic and aqueous extracts of fruits, leaves and root barks of *G. asiatica* showed significant activity at doses 200 and 400 mg/kg in mice and rats than other tested doses (doses 125, 250 and 500 mg/kg) (Akhtar et al., 2016; Paviaya et al., 2013; Qamar et al., 2020). Qamar et al., (2020) have been also studied hexane, DCM, methanolic and 50% methanolic extracts of fruits of *G. asiatica*. Similarly, 50% hydro-methanolic extract showed significant activity at dose 400 mg/kg b.w. due to high total phenolic contents. Similarly, the aqueous extract of leaves of *G. tiliaefolia* showed a significant effect at dose 500 mg/kg due to the reduction of leukocyte counts (Juvekar et al., 2007). Anti-inflammatory activity has been reported in flavonoids (**9, 13-14, 18, 22, 34-35, 43, 45, 48** and **53**), isoflavonoids (**73**), phenol (**85**), phenolic acid (**85**), hydroxycinnamic acid (**104**) and terpenoids (**110-113, 116** and **118-119**) and steroids (**123** and **125**) which were identified and isolated from this genus (Du et al., 2018; Imran et al., 2019; Jayasinghe et al., 2004; Lin et al.,2018; Li et al., 2017; Prakash et al., 2019; Zheng et al., 2017).

### 5.6. Antimalarial activity

The methanolic extract of leaves of *G. asiatica* showed significant antimalarial activity at doses 50 and 100 mg/kg due to bioactive compounds (Zia-Ul-Haq et al., 2012b). Ma et al., (2006) have been screen 12 compounds *in-vitro* antimalarial activity against *Plasmodium falciparum* (*P. falciparum*). All these 12 compounds showed $IC_{50}$ < 10 µg/mL. Neolignans (**78-81**), coumarinolignans (**82** and **84**), quinone (**109**) and triterpenes (**117** and **120**) showed varying degrees of antimalarial effects (Ma. et al., 2006).

### 5.7. Antimicrobial activity

Many researchers tested the antimicrobial activity in ethanolic extracts of different parts of *Grewia venusta* Fresen., *G. paniculata, G. asiatica*, and *G. mollis* against different microbes such as *Bacillus cereus, Bacillus subtilis, Candida albicans, Escherichia coli, Klebsiella pneumonia, Pseudomonas aeruginosa, Pseudomonas aureus, Staphylococcus aureus, Shigella dysenteriae* (Kubmarawa et al., 2007; Naqvi et al., 2012; Nasrin et al., 2015; Shagal et al., 2012). The ethanolic extract of stem bark showed the highest effect against S. dysenteriae with the zone of inhibition of 23±1.63 and 23±1.77 mm, respectively at 400 µg/disc (Nasrin et al., 2015). Similarly, ethanolic extracts of roots, stem bark and leaves of *G. mollis* have been reported significant activity against *E. coli, S. aureus* and *Streptococcus* species than water extracts (Shagal et al., 2012). In contrast, acetone extract of leaves of *G. orientalis* showed high activity against *E. coli, B. subtilis, S. aureus, P. aeruginosa* and *K. pneumonia* than methanolic and ethanolic extracts with minimum inhibitory concentration (MIC) ranged from 50-250 µg/mL (Prathyusha et al., 2013). The methanolic and ethyl acetate extracts of leaves of *Grewia plagiophylla* K. Schum exhibited substantial effects against *S. aureus*. The methanolic extract exhibited a zone of inhibition of 20 mm against *Salmonella typhi*. The ethanolic extracts were inactive against all tested microbial at various concentrations (Douglas & Gitonga, 2016). The MIC values of methanolic extract of *G. tiliaefolia* were found to be 125, 31.25 and 62.5 µg/mL against *Bacillus stearothermophilus, L. licjmani* and *Pseudomonas*

*cepacia*, respectively (Ramshankar et al., 2008). The methanolic extract of *G. asiatica* fruits, its phenolic acids, flavanols and flavonols fractions showed significant antimicrobial effect against *B. subtilis, S. aureus, Staphylococcus epidermidis* and *Klebsiella pneumonia* except anthocyanins fraction (Siddiqi et al., 2011). The aqueous (water), methanolic and hydro-alcoholic extracts of roots of *G. asiatica, G. tiliifolia*, and *G. tenax* showed significant activity against *P. aeruginosa, B. subtilis, S. aureus, E. coli*, and *K. pneumonia*. The hydro-alcoholic extract of *G. asiatica* was found the most effective against *K. pneumoniae* (MIC=3.90 μg/mL) followed by *C. albicans* (MIC=31.2 μg/mL) and *A. fumigatus* (MIC=31.2 μg/mL). *G. tenax* and *G. tiliifolia* extracts exhibited remarkable potential against *B. subtilis* and *E. coli*, respectively (Sharma et al., 2016). The methanolic, *n*-hexane and ethyl acetate extracts of leaf gave satisfactory inhibitory activities against *S. aureus, E. coli, B. subtilis, P. aeruginosa, S. typhii, K. pneumonae, C. albicans, Aspergillus niger, Penicillium notatum* and *Rhizopus stolonifer* except ethyl acetate extract which exhibited no effects against P. notatum and R. stolonifer (Hamid et al., 2016). *In-vitro* antibacterial activity of the methanolic, chloroform and hexane extracts of the leaves and stem bark of *G. lasiocarpa* respectively have been tested against *E. coli,* P. aeruginosa, *S. aureus, K. pneumonia* and *Salmonella typhimurium* by agar-well diffusion method. The hexane extracts of the leaves and stem bark showed a remarkable inhibitory effect against S. *aureus* (Akwu et al., 2019). The acetone extracts of the leaves and roots of *Grewia flava* DC exhibited the better activity than methanolic, acetyl acetate, and water extracts with MIC values 0.03 mg/mL against *S. aureus* and *S. typhimurium* and 0.07 mg/mL against *B. cereus, E.coli* and *S. aureus* (Lamola et al., 2017). The methanolic, water, petroleum ether and isopropanol extracts of *G. tenax* showed variable degrees of inhibitory activity against *E. coli, S. marcescens, K. pneumoniae, S. typhi, P. aeruginosa* and *P. vulgaris, S. aureus, Enterococcus fecalis, S. epidermidis, S. pneumoniae* and *B. subtilis* at 1 mg/mL. The results exhibited that the all extracts have very good inhibition against *S. pneumoniae* and *S. typhi* and moderate inhibition against *E. fecalis, S. epidermidis*, and *P. aeruginosa* while inactive against *E. coli, S. aureus, S. marcescens, K. pneumoniae, B. subtilis* and *P. vulgaris* (Aadesariya et al., 2017a). The methanolic extract of *G. occidentalis* showed significant inhibition against *B. cereus, B. pumilus, B. subtilis, Micrococcus kristinae, S. aureus, Enterobacter cloacae, E. coli, K. pneumonia, P. aeruginos* and *Serratia marcescens* than water and acetone extracts (Grierson & Afolayan, 1999). The methanolic, DCM, acetone and *n*-hexane extracts of leaves of *G. flava* showed significant activity against *S. aureus, E. faecaelis, E. coli* and *P. aeruginosa* (Gololo et al., 2016). The acetone extracts of twigs and leaves have been reported for significant effects against *Aspergillus fumigates, A. niger, Candida glabrata, Trichophyton* sp., *Geotrichum* spp. *Microsporum gypsium, Penicillium sp*. (Afolayan et al., 2002; Goswami et al., 2018). Flavonoids (**9, 22** and **43**), phenol (**85**), phenolic acid (**97**), hydroxycinnamic acids (**100** and **104**) and volatile compounds (**112-113, 151, 170, 184** and **198**) showed antimalarial activity.

### 5.8. Antipyretic/antinociceptive activity

The antipyretic activity has been reported in leaves and fruits (aqueous extract) of *G. tiliaefolia* and *G. asiatica* (methanolic, aqueous), respectively at 500 mg/kg (Akhtar et al., 2016; Sakat & Juvekar, 2009). The significant antinociceptive activity has been reported in hexane, DCM, methanolic and 50% methanolic of fruits *G. asiatica* at 3.1–7.9 mg/kg b.w. (Qamar et al., 2020).76 Aqueous extract of leaves of *G. tiliaefolia* has possessed comparable significantly antipyretic activity at 250 and 500 mg/kg (Sakat & Juvekar, 2009). Compounds **104, 118** and **119** showed antipyretic activity whereas antinociceptive effects were observed in compounds **116, 118** and **170** which have been reported in genus *Grewia* (Geetha & Jayasinghe et al., 2004; Tsai et al., 2016; Geetha and Varalakshmi, 2001).

### 5.9. Antioxidant activity

The ethanolic extracts of leaves, stems, and fruits of *G. bicolar* and *Grewia* carpinifolia Juss. showed the free radical scavenging property at different concentrations using 1,1-diphenyl-2-picrylhydroxyl (DPPH), 2,2'-azinobis-3-ethylbenzothiozoline-6-sulfonic acid (ABTS), ferric reducing antioxidant power (FRAP) assay. All extracts of *G. carpinifolia* were found to more effective by scavenging the ABTS radical assay and significant antioxidant activity was also reported in *G. bicolar* at a concentration of 200 mg/L (Adebiyi et al., 2017; Gwatidzo et al., 2018). The ethanolic extract of *G. serrulata* showed strong free radical scavenging property with their $IC_{50}$ values in DPPH (9.16 ±1.05 mg/mL), superoxide (35.59 ±1.6805 mg/mL) and nitric oxide (151.80 ±1.79 mg/mL) (Chandiran et al., 2013a). In contrast, methanolic, ethanol and acetone extracts of leaves of *G. tenax* showed significant scavenging activity than ethyl acetate and acetonitrile *n*-hexane, benzene, chloroform, petroleum ether and isopropanol extracts. Similarly, its methanolic and ethanolic extracts showed higher scavenging activities with their $IC_{50}$ values of DPPH at 0.023, 0.072, 0.167, 0.259 and 0.317, respectively (Aadesariya et al., 2017c).

The methanolic extracts of *G. asiatica* fruits and leaves of *G. nervosa, G. optiva, G. abutilifolia, G. mollis* and *G. tiliaefolia* showed significant scavenging activity using DPPH and ABTS assay (Ahammed et al., 2018; Siddiqi et al., 2013). Flavanol fraction in *G. asiatica* showed considerable DPPH scavenging activity (Siddiqi et al., 2013) whereas ethyl acetate fraction ($IC_{50}$ = 33.46 μg/mL) of methanolic of *G. nervosa* leaf showed the high scavenging activity than petroleum ether, chloroform, ethyl acetate and aqueous fractions (Rehman et al., 2013; Ahammed et al., 2018). Petroleum ether fraction showed high radical scavenging activity in the DPPH assay ($IC_{50}$ = 3.82 ± 0.055 μg/mL) and hydroxyl radical scavenging assay ($IC_{50}$ 6.45 ± 1.297 μg/mL). Highest radical scavenging potential ($IC_{50}$ = 15.62 ±1.31 μg/mL) was observed chloroform fraction (Salam, & Rafe, 2019). The methanolic extract of *G. tiliaefolia* leaves showed significant free radical scavenging activity at the $IC_{50}$ value of 71.5 ± 1.12 μg/mL (Malar et al., 2017). The 95% methanolic and ethyl acetate extracts showed the highest free radical scavenging property on DPPH and ABTS radicals assay with their respective $IC_{50}$ values 75 and 88 μg/mL. The ethyl acetate fraction showed higher inhibition of radicals with an $IC_{50}$ value of 380 μg/mL than other tested fractions. Chloroform and aqueous fractions exhibited significant activity with $IC_{50}$ values at 380 and 390 μg/mL, respectively, whereas the *n*-hexane fraction was inactive (Zahoor et al., 2020). The 80% methanolic extract of *G. pubescens* leaves reported for promising antioxidant activity and its aqueous fraction had high activity followed by methanolic extract though chloroform fraction was inactive using ABTS assay (Anwar et al., 2015). Acetone extracts of *G. flava* and *G. asiatica* leaf showed the significant free radical scavenging activity than methanolic, acetyl acetate and water extracts with $LC_{50}$ (lowest toxicity) of 551.68 and 127.5 μg/mL using the DPPH assay (Goswami et al., 2018; Lamola et al., 2017). The methanolic extracts of the leaves and stem bark of *G. lasiocarpa* showed the promising antioxidant activity with $IC_{50}$ values of 0.02 and 1.34 μg/mL, respectively in DPPH assay, while for ferric reducing power (FRAP), the methanolic and chloroform extracts of leaves and stem have been reported for high reducing power with $IC_{50}$ values of 9.76 and 12 μg/mL, respectively due to the highest phenolic content (Akwu et al., 2019). The high antioxidant activity was observed in aqueous and methanolic extracts of *G. tenax* and hydroalcoholic extract of *G. asiatica* while lowest in *G. tiliifolia* using FRAP, DPPH, ABTS and NO radical scavenging assay due to highest total phenolic content (Sharma et al., 2016). Methanolic extract of the stem bark of *G. optiva* showed significant free radical scavenging effect than *n*-butanol, ethyl acetate and chloroform extracts with $IC_{50}$ value of 10.26 μM, using the DPPH assay (Hamid et al., 2016). Hydroalcoholic extracts of the stem and root of *G. serrulata* and leaf and bark of *G. nervosa* showed high potential with greater $IC_{50}$ values of stem (42.91±0.88) and root (53.87 ±0.35) than leaf (126.73±1.20) of *G. serrulata* and bark (88.87±1.25) of

*G. nervosa* (Ramesh & Rao, 2018). Typically, flavonoids (**14, 18, 22, 34, 38, 43, 46, 50, 51, 54, 56, 58, 59, 60** and **64-66**), isoflavonoids (**73** and **77**), phenolic acid (**96** and **97**), hydroxycinnamic acid (**100** and **103-104**), hydrolyzable tannin (**106-107)** and volatile compounds (**110-113, 116, 170, 195-196, 198** and **226**) reported in *Grewia* species also showed antioxidant activity (Koley et al., 2020; Singh et al., 2010).

### 5.10. Antiplatelet activity

The methanolic extracts of *G. asiatica* leaves showed significant platelet aggregation inhibition activity. More than 50% inhibition was observed at 5 mg/mL along with the dose at 10 mg/mL showed maximum inhibition about 93% ($IC_{50}$ = 4.85 mg/mL) (Zia-Ul-Haq et al., 2012a). The methanolic extracts of leaves of *G. tiliaefolia* showed significant anti-aggregation activity by preventing the oligomerization (Malar et al., 2017). Compounds **34, 43** and **116** showed antiplatelet activity reported in *Grewia* species (Cardoso et al., 2018; Imran et al., 2019; Wang et al., 2019).

### 5.11. Hepatoprotective activity

The methanolic extracts of *G. mollis* (leaves) and *G. asiatica* (fruits) showed significant hepatoprotective effects in rats at doses 700 and 5 mg/kg stress by radiation and CCl4. The result showed that a significant reduction of the serum levels of bilirubin, aspartate aminotransferase and alanine aminotransferase (Asuku et al., 2012; Sharma and Sisodia, 2010a). Both, 80% methanolic and water extracts of *G. tenax* fruits showed significant protective effects at 25 and 50 µg/mL and 12.5 and 100 µg/mL, respectively (Saleh et al., 2015). The ethanolic extracts of leaves of *G. carpinifolia* and *G. asiatica* were significantly restored and normalized elevated liver enzymes such as serum glutamate pyruvate transminase (SGPT), serum glutamate oxaloacetate transaminase (SGOT), serum alkaline phosphatase (ALP) total bilirubin, sphincter of oddi dysfunction (SOD) and catalase at doses 100 and 200 mg/kg on induced hepatic damage rats (Adebiyi & Olayemi, 2018; Dwivedi and Manigauha, 2017). The significant hepatoprotective activity has been reported in ethanolic extracts of *G. umbellifera* bark at a dose of 200 mg/kg on paracetamol-induced rats than petroleum ether, benzene, chloroform, acetone, ethyl acetate, and water.59 95% ethanolic extracts of *G. hirsute* root was significantly restored and normalized elevated serum enzymatic levels of SGPT, SGOT, ALP, total bilirubin, SOD, and catalase at a dose of 250, 750 mg/kg on ethylene glycol induced hepatic damage in rats (Basha et al., 2015). Similar results were also observed in 96% ethanol of *G. tenax* fruits at doses 250 and 500 mg/kg on $CCl_4$ induced oxidative stress and hepatotoxicity in rats (Al-Said et al., 2011). The observed all hepatoprotective effects could be due to phenolic content in *Grewia* genus. Compounds **63, 104, 114, 116**, and **118** have been reported for hepatoprotective activity (Adisakwattana et al., 2009; Cardoso et al., 2018; Jayasinghe et al., 2004; Mulholland et al., 2002; Tsai et al., 2016).

### 5.12. Nephroprotective activity

The ethanolic extract of barks of *G. umbellifera* showed significant nephroprotective effects at dose 200 mg/kg in nephrotoxin induced rats than petroleum ether, benzene, chloroform, acetone, ethyl acetate, and distilled water extracts due to reduction of the levels of urea, creatinine, uric acid, phosphorous, magnesium, sodium, and chloride significantly (Selvaraj et al., 2017). Compound **118** showed a nephroprotective effect (Geetha & Jayasinghe et al., 2004; Tsai et al., 2016; Geetha and Varalakshmi, 2001).

### 5.13. Neuroprotective activity

The ethanolic extract of *G. paniculata* showed significant neuroprotective effect by reduction of locomotors and exploratory in mice at the doses of 250 and 500 mg/kg, b. w. (Ali et al., 2015). The aqueous fraction of *G. abutilifolia* leaf showed high inhibition of acetylcholinesterase with $IC_{50} = 5.73 \pm 0.59$ µg/mL, although the highest inhibition of butyrylcholinesterase exhibited by petroleum ether fraction with $IC_{50} = 6.57 \pm 1.81$ µg/mL in a dose-dependent manner. The chloroform fraction was shown the highest activity with 25.75 ± 1.62% in clot test. The above results showed that the effectiveness of *G. paniculata* and *G. abutilifolia* against neurological diseases (Rafe et al., 2018). Methanolic extract of *G. tiliaefolia* showed significant dual cholinesterase inhibition with $IC_{50}$ = 64.26±2.56 and 54±0.7 µg/mL for acetyl and butyrylcholinesterase (BChE), respectively. Besides, methanolic extract has increased the viability of Neuro2a cells up to 95% against Ab25-35 neurotoxicity (Malar et al., 2017). The major constituent (1) in an *n*-butanol fraction of methanolic root extract was found to possess the dose-dependent $\alpha$-glucosidase inhibition activity with an $IC_{50}$ = 53.40 µM. Moreover, it showed maximum $\alpha$-glucosidase inhibition was 97.48 ± 0.7% at 107.5 µM, which was approximately 1.3 × 103 fold higher than the activity shown by standard acarbose (97.72 % inhibition at 61.95 mM). $\beta$-carboline alkaloids (**5-7**) showed sedative activities (Jaspers et al., 1986; Malar et al., 2017; Meena et al., 2017a). Compounds **13, 50, 100, 104**, and **118** also exhibited neuroprotective activity (Geetha and Varalakshmi, 2001; Jayasinghe et al., 2004; Naveed et al., 2018; Spagnol et al., 2019; Tsai et al., 2016).

### 5.14. Radioprotective activity

The methanolic extracts of *G. asiatica* fruits showed prophylactic action against γradiation-induced metabolic disorders in mice at an optimised dose 700 mg/kg due to noticeably elevation of the glutathione, glutathione peroxidase, sugar, and protein levels along with degradation of peroxidation and cholesterol level in serum, brain, cerebrum, and liver (Ahaskar et al., 2007a; Ahaskar et al., 2007b; Ahaskar & Sisodia, 2006; Sharma et al., 2007; Sharma & Sisodia, 2010b; Singh et al., 2007). Anthocyanin (**63**) can protect from a range of radiations (Adisakwattana et al., 2009; Ullah et al., 2012).

### 5.15. Uterotonic activity

The aqueous extracts of *G. occidentalis* wood showed to causes contraction in the uterine muscle of guinea pig due to compounds **94** and **114**. Both compounds **94** and **114** were stimulated moderate uterotonic activity at a cumulated dose 250 and multiples five of 366 µg, respectively. Thus, compound **114** was interesting and seems to suggest a sensitisation of the uterine muscle tissues. Compounds **87, 95**, and **115** also exhibited uterotonic activity (Mulholland et al., 2002).

### 5.16. Wound healing properties

The polysaccharides extract of inner bark of *G. mollis* has been reported for significant wound healing effects on $COL_1A_1$ transcription, collagen deposition and cell migration in 3T3 fibroblasts via in vivo study. Unmodified and destarched *Grewia* gum of polysaccharide extracts were tested but high potential was observed in Unmodified *Grewia* gum of polysaccharide extract (Pearman et al., 2019). The methanolic extract of stem bark of *G. tiliaefolia* and its gulonic acid $_\gamma$-lactone with $LD_{50}$ values have been reported at 1000 and 600 mg/kg b.w., respectively. The extract showed significant reduction in the wound area (95.71%) with a faster rate of epithelialisation (18.40 ± 0.16) (Ahamed et al., 2010).

## 6. Toxicity

Although genus *Grewia* has been studied in the form of extracts, fractions, and isolated chemical compounds with various pharmacological activities, no study had reported any toxicity for this plant and fruits are edible while leaves are used as fodder (Dhawan et al., 1977;

**Table 6**
Biological activities of different extracts and its fractions of genus *Grewia*.

| S. no. | Activity | Extract | Plant part | Species | Dose | Results | Reference |
|---|---|---|---|---|---|---|---|
| 1. | Analgesic | Methanolic and aqueous | Fruits | *G. asiatica* | 125, 250, 500 mg/kg | Aqueous and methanolic extracts of *G. asiatica* fruit showed significant analgesic activity. | Akhtar et al. (2016) |
| | | Aqueous | Leaves | *G. tiliaefolia* | 250, 500 mg/kg | The aqueous extract of leaves of *G. tiliaefolia* possessed analgesic activity. | Sakat & Juvekar (2009) |
| | | Butanol, ethyl acetate, chloroform and hexane, | Leaves | *G. crenata* | 50, 100, 200 mg/kg | All extracts of *G. crenata* showed significant analgesic activity. | Ukwuani et al. (2014) |
| 2. | Anticancer | Ethanolic | Leaves and bark | *G. paniculata* | 1.25-320 µg/mL | Ethanolic extracts of *G. paniculata* were moderately toxic. | Nasrin et al. (2015) |
| | | Methanolic | Leaves | *G. asiatica* | 0.5, 1, 10, 50, 100, 200 µg/mL | Methanolic extract showed significant cytotoxic effect against HL – 60, K – 562, MCF – 7 and Hela cancer cell lines and anticancer activity against Ehrlich's ascites carcinoma (EAC) cell lines | Kakoti et al. (2011) |
| | | Methanolic | Whole | *G. tiliaefolia* | | Methanolic extract of *G. tiliaefolia* showed moderately cytotoxic against for Vero and HEp-2 cell lines. | Ramshankar et al. (2008) |
| | | Methanolic | Leaf | *G. nervosa* | 200, 400 µg/mL | The methanolic leaf extract of *G. nervosa* showed against MCF-7 breast cancer cell line. | Meena et al. (2017b) |
| | | 95% methanolic | Stems and roots | *G. optiva* | 200, 300, 400, 500 mg/kg | 95% Methanolic extract was found to be nontoxic for tested cell lines. | Zahoor et al. (2020) |
| | | Methanolic, aqueous, acetyl acetate and acetone | Berries, leaves, bark and roots | *G. flava* | 402.13- 551.68 µg/mL | The results showed that the extracts of *G. flava* are less toxic to Vero cells. | Lamola et al. (2017) |
| | | Methanolic, chloroform and hexane, | Leaves and stem bark | *G. lasiocarpa* | 0.625, 1.25, 2.5, 5, 10 mg/mL | The cytotoxicity of the plant was relatively low. | Akwu et al. (2019) |
| | | Methanolic, 50% methanolic dichloromethane and hexane | Fruit | *G. asiatica* | 0.5–200 µg/mL | 50% Hydro-methanolic extract of *G. asiatica* fruits showed maximum cytotoxic activity. | Qamar et al. (2020) |
| | | Aqueous | Fruits and leaves | *G. asiatica* | 0.01-100 µg/mL | Aqueous leaf and fruit extract of *G. asiatica* possessed in-vitro cytotoxic activity on epidermal kidney, cell lung, cervical, laryngeal and breast cancer cell lines | Marya et al. (2011) |
| | 3. Antidiabetic | Ethanolic | Aerial parts | *G. serrulata* | 5-100 mg | Ethanolic extracts of aerial parts antidiabetic activity. | Chandiran et al. (2013) |
| | | Ethanolic | Fruit | *G. asiatica* | 100, 200 mg/kg | *G. asiatica* fruit extract showed antidiabetic activity against STZ-induced hyperglycemia. | Khattab et al. (2015) |
| | | Ethanolic | Leaves | *G. asiatica* | 100, 200, 400 mg/kg | The ethanolic extracts of *G. asiatica* at dose of 400 mg/kg enhanced the antihyperglycemic activity. | Khattab et al. (2015) |
| | | Ethanolic | Stem barks | *G. asiatica* | 200, 400 mg/kg | Ethanol extract of *G. asiatica* stem barks showed antidiabetic activity in diabetic rats | Khatune et al. (2016) |
| | | Ethanolic and aqueous | Aerial parts | *G. serrulata* | 200, 400 mg/kg | The ethanolic extract of aerial parts showed good hypoglycemic activity. | Chandiran et al. (2013) |
| | | Methanolic | Leaves | *G. asiatica* | 100, 250, 500 mg/kg | The methanolic extracts of leaves of *G. asiatica* possessed antidiabetic activity. | Zia-Ul-Haq et al. (2012b) |
| | | 95% methanolic | Stems and roots | *G. optiva* | 200, 300, 400 and 500 mg/kg | The methanolic extract of *G. optiva* showed antidiabetic and antihyperlipidemic activity in Swiss albino mice. | Zahoor et al. (2020) |
| | | | Bark | *G. herbacium, G. asiatica,* and *G. sylvestre* | 20,10, 5g/Kg | Dose at 5g/Kg showed significant reduction of cholesterol and triglycerides all tested Grewia spp. | Dogar et al. (1988) |
| 4. | Antiemetic | Methanolic | Leaves | *G. asiatica* | 50, 100 mg/kg | The methanolic extracts of leaves of *G. asiatica* possessed antiemetic activity. | Zia-Ul-Haq et al. (2012b) |
| | | 70% aqueous methanolic | Root | *G. lasiodiscus* | 50, 100, 200 mg/kg | The aqueous and methanolic extracts of *G. lasiodiscus* root and its fractions showed antiemetic activity. | Tijani et al. (2008) |
| | | Methanolic and aqueous | Fruit | *G. asiatica* | 125, 250, 500 | Aqueous and methanolic extracts of *G.* asiatica fruit showed significant antiinflammatory activities. | Akhtar et al. (2016) |
| | | | Fruit | *G. asiatica* | 200, 400 mg/kg | | |

(*continued on next page*)

**Table 6** (*continued*)

| S. no. | Activity | Extract | Plant part | Species | Dose | Results | Reference |
|---|---|---|---|---|---|---|---|
| | | Methanolic, 50% methanolic, dichloromethane, and hexane, | | | | *G. asiatica* fruit extracts showed significant antiinflammatory activity. | Qamar et al. (2020) |
| | | Aqueous | Leaves | *G. tiliaefolia* | 250, 500mg/kg | Leaves of *G. tiliaefolia* possessed antiinflammatory activity. | Juvekar et al. (2007) |
| 6. | Antimalarial | Methanolic | Leaves | *G. asiatica* | 50, 100 mg/kg | The methanolic extracts of leaves of *G. asiatica* possessed antimalarial activity. | Zia-Ul-Haq et al. (2012b) |
| | | 3*r*,20-lupandiol, grewin, nitidanin, 2*r*,3*α*-dihydroxy-olean-12-en-28-oic acid, and 2,6-dimethoxy-1-acetonylquinol | Leaves, twigs and stems | *G. bilamellata* | $IC_{50} < 10$μg/mL | All tested compounds showed *in vitro* antimalarial activity against *Plasmodium falciparum.* | Ma. et al. (2006) |
| | | Ethanolic | Leaves and bark | *G. paniculata* | 400 μg/disc | Ethanolic extracts of *G. paniculata* have potent antibacterial activity. | Nasrin et al. (2015) |
| | | Ethanolic | Fruit, barks and leaves | *G. asiatica* | 5mg/mL | Ethanolic extracts of plant parts of *G. asiatica* showed antibacterial activity. | Naqvi et al. (2012) |
| | | Ethanolic and aqueous | Roots, stem-bark and leaves | *G. mollis* | | Ethanol extracts showed better activity against *E. coli, S. aureus* and *Streptococcus* sp. | Shagal et al. (2012) |
| | | Methanolic, ethanolic and acetone | Leaves | *G. orientalis* | 50-250 μg/mL | The acetone extract of leaves of *G. orientalis* showed high activity than other extracts. | Prathyusha et al. (2013) |
| | | Methanolic | Whole plant and bark | *G. tiliaefolia* | 31.25, 62.5, 125, 250 mg/mL | *G. tiliaefolia* had good antimicrobial activity against *L. Licjmani*> *P. Cepacia*> *B. Sterarothermophilus*. | Ramshankar et al. (2008) |
| | | Methanolic | Fruits | *G. asiatica* | 100 μg/mL | Crude extract of *G. asiatica* substantially showed antimicrobial activity against tested pathogens. | Siddiqi et al. (2011) |
| | | Methanolic, hydro alcoholic and aqueous | Roots | *G. asiatica,G. tiliifolia* and *G. tenax* | - | The hydroalcoholic extract of roots of *G. asiatica* and *G. tenax* showed better antimicrobial activity. | Sharma et al. (2016) |
| | | Methanolic, ethyl acetate, | Leaves | *G. pubescens* | 6.25, 12.5, 25, 50, 100, 200 | Methanolic extract of the plant has been possessed significant antimicrobial activity. | Hamid et al. (2016) |
| | | Chloroform and hexane | Leaves, stem and bark | *G. lasiocarpa* | 200, 100, 50, 25, 12.5, 6.25 mg/mL | The methanolic and chloroform extracts of *G. lasiocarpa* leaves and stem bark showed potential antibacterial activity | Akwu et al. (2019) |
| | | Methanolic, aqueous acetone and acetyl acetate | Berries, leaves, bark and roots | *G. flava* | 2.5-0.03 mg/mL | Root and leaves extracts showed significant antibacterial activity mainly against *Staphylococcus aureus*. | Lamola et al. (2017) |
| | | Acetone | Twig and leaves | *G. occidentalis* | 0.1-10 mg/mL | *G. occidentalis* showed least activity. | Afolayan et al. (2002) |
| 8. | Antinociceptive | Methanolic, 50% methanolic, dichloromethane and hexane, | Fruits | *G. asiatica* | 200, 400 mg/kg | Methanolic and 50% hydro-methanolic showed antinociceptive activity. | Qamar et al. (2020) |
| 9. | Antioxidant | Ethanol | Fruits | *G. bicolar* | 200, 100, 50, 10, and 5 mg/L | *G. bicolar* showed significant antioxidant activity of over 80% at a concentration of 200 mg/mL. | Gwatidzo et al. (2018) |
| | | Ethanolic and aqueous | Aerial parts | *G. serrulata* | | The ethanolic extract of aerial parts of *G. serrulata* was possessing strong antioxidant activity. | Chandiran et al. (2013) |
| | | Methanolic | Fruits | *G. asiatica* | 5-50 ppm | Methanolic extract of *G. asiatica* showed potent radical-scavenging activity. | Siddiqi et al., (2013) |
| | | Methanolic | Leaves | *G. optiva* | 0, 50, 100, 150, 250, 500 mg/L | *G. optiva* showed considered antioxidant activity. | Rehman et al. (2013) |
| | | Methanolic | Leaves | *G. tiliaefolia* | 100–500 μg/mL | Methanolic extract of *G. tiliaefolia* leaves showed significant free radical scavenging activity. | Malar et al. (2017) |
| | | Methanolic | Leaves | *G. mollis* | 5 mg/kg | Crude extract of *G. mollis* leaves showed potent antioxidant activity. | Asuku et al. (2012) |
| | | Methanolic | Whole | *G. tiliaefolia* | 50,100,150 | Crude extract of *G. tiliaefolia* showed good antioxidant activity. | Ramshankar et al. (2008) |
| | | 95% methanolic | Stems and roots | *G. optiva* | 62.5, 125, 250, 500, 1000 μg/mL | 95% Methanolic of *G. optiva* showed good antioxidant activity. | Zahoor et al. (2020) |
| | | Methanolic, aqueous acetyl acetate and acetone | Berries, leaves, | *G. flava* | 3.9–500 μg/mL | The acetone extracts showed good free radical scavenging activity. | Lamola et al. (2017) |

(*continued on next page*)

**Table 6** (*continued*)

| S. no. | Activity | Extract | Plant part | Species | Dose | Results | Reference |
|---|---|---|---|---|---|---|---|
| | | | bark and roots | | | | |
| | | Methanolic, chloroform and hexane | Leaves and stem bark | *G. lasiocarpa* | 15, 30, 60, 120 and 240μg/mL | The methanolic and chloroform extracts of *G. lasiocarpa* leaves and stem bark showed potential source of natural antioxidants. | Akwu et al. (2019) |
| | | Methanolic, aqueous and hydroalcoholic | Roots | *G. asiatica,G. tiliifolia,* and *G. tenax* | | Crude extracts of *G. tenax* showed highest antioxidant activity whereas lowest in *G. tiliifolia*. | Sharma et al. (2016) |
| 10. | Antiplatelet | Methanolic | Leaves | *G. asiatica* | 1-10 mg/mL | Methanolic extracts of *G. asiatica* leaves showed potent platelet aggregation inhibition activity. | Zia-Ul-Haq et al. (2002a) |
| | | Methanolic, aqueous, ethyl acetate, chloroform and petroleum ether | Leaves | *G. tiliaefolia* | 100-500 μg/mL | Methanolic extracts of leaves of *G. tiliaefolia* showed significant anti-aggregation activity. | Malar et al. (2017) |
| 11. | Antipyretic | Aqueous | Leaves | *G. tiliaefolia* | 250, 500 mg/kg | The aqueous extract of leaves of *G. tiliaefolia* possessed analgesic activity. | Sakat & Juvekar (2009) |
| 12. | Antipyretic | Methanolic and aqueous | Fruits | *G. asiatica* | 125, 250, 500 mg/kg | Aqueous and methanolic extracts of *G. asiatica* fruit showed significant . antipyretic activity. | Akhtar et al. (2016) |
| 13. | Hepatoprotective | Methanolic | Leaves | *G. mollis* | 5 mg/kg | The methanolic extract of *G. mollis* leaves showed a significant hepatoprotective effects. | Asuku et al. (2012) |
| | | Methanolic | Fruit | *G. asiatica* | 100, 400, 700, 1000, 1300 mg/kg | Methanolic extract of *G. asiatica* showed good potential against radiations. | Sharma, & Sisodia (2010a) |
| | | 96% ethanolic | Fruit | *G. tenax* | 250, 500 mg/kg | 96% Ethanol showed ameliorative effect on $CCl_4$–Induced oxidative stress and hepatotoxicity in rats | Al-Said et al. (2011) |
| | | Aqueous, chloroform and petroleum ether | Leaf | *G. abutilifolia* | 7.125-250 μg/mL | Aqueous and petroleum ether extracts showed highest inhibition of acetylcholinesterase and butyrylcholinesterase, respectively. | Rafe et al. (2018) |
| | | Methanolic | Leaves | *G. tiliaefolia* | 100-500 μg/mL | Methanolic extract of *G. tiliaefolia* showed significant dual cholinesterase inhibition. | Malar et al. (2017) |
| 15. | Radioprotective | Methanolic | Fruits | *G. asiatica* | 100,400,700,1000,1300 mg/kg | Methanolic extracts of *G. asiatica* showed significant prophylactic action against radiation-induced metabolic disorders. | Sharma et al. (2007) |
| | | Methanolic | Fruits | *G. asiatica* | (100, 400, 700, 1000, 1300 mg/kg | Methanolic extracts of *G. asiatica* showed strong radioprotective effect in in Mice testis. | Sharma & Sisodia (2010b) |
| | | Methanolic | Fruits | *G. asiatica* | 100, 400, 700, 1000, 1300 mg/kg | Methanolic extracts of *G. asiatica* showed strong radioprotective effect in in mice. | Singh et al. (2007) |
| 16 | Uterotonic | Aqueous andconiferaldehyde | Bark and wood | *G. occidentalis* | 500μg (2 × 250 μg) | Aqueous extract showed significant uterotonic activity in guinea pig. | Mulholland et al. (2002) |

Dev et al., 2019; Khan & Hanif, 2006; Mehmood et al., 2020; Naqvi et al., 2012). Chandiran et al., (2013c) have been found that the aqueous and ethanolic extracts of aerial parts of *G. serrulata* is safe and non-toxic greater than 800 mg/kg in rats. Similarly, hydro-methanolic leaves extracts of G. crenata were safe and non-toxic upto doses3600 mg/kg in rats (Ukwuani et al., 2012). Similarly, ethnobotanical surveys did not mention any toxicity associated with the use of this plant. Still, there may be inadequate evidence to overrule the toxicity and safety of this plant. Hence, further in-depth *in-vitro* and in vivo studies for toxicity must be considered.

## 7. Conclusions and future perspectives

The genus *Grewia* is a group of excellent medicinal and commercial valued plants with high demands in the fields of chemical, beverage, and pharmaceutical industries. Most of the diverse types of chemical compounds are widely found in alcoholic extracts of fruits and leaves of the *G. asiatica, G. bicolour, G. bilamellata, G. damine, G. flavescens, G. lasiocarpa, G. nervosa, G. occidentalis, G. optiva, G. tiliaefolia* and *G. villosa*. Modern pharmacological studies confirmed that the genus *Grewia* has a wide range of pharmacological activities of chemical compounds and their extracts/fractions. However, several aspects required to further explore and investigate (1) as previously, more research has been conducted only on commonly well-known species such *G. asiatica, G. optiva* and *G. lasiocarpa*, instead of them they are required to investigate those species which have a lack of studies; (2) only few work has been reported on the root extracts of this genus; (3) validated medicinal properties of several chemical compounds in genus *Grewia* remain unknown till date; (4) there is need to isolate phytochemicals on the large scale from plant genus *Grewia* to explore their biological activities and mechanism for therapeutic potential; (5) pre-clinically studies of known chemical compounds needs to be explored for clinical trials, especially flavonoids, alkaloids and neolignans (6) more than 227 chemical compounds have been reported, while only a very few have been explored for their biological activities and pre-clinical studies. Overall, there is a requirement for further systematic and deep studies on the biological as well as chemical aspects of plants of the genus *Grewia* to develop lead compounds with high biological potential. The long history of traditional uses, a wide range of biological properties and toxicity studies indicated that the plant of genus *Grewia* could be safe and significant for clinical

applications. The present compilation of chemical compounds along with their biological activities will be helpful in future studies on this genus for search of new lead compounds for drug discovery. Table 6

## CRediT authorship contribution statement

Sunil Kumar conceived the idea, designed, collected data, compiled including tables, chemical structures, graphical abstract using power point presentation and ChemDraw pro software and wrote the manuscript. Bikrma Singh and Vikas Bajpai. helped in editing the manuscript.

## Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Supplementary materials

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