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## Pharmacological actions and potential uses of *Grewia asiatica*: A review

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### Abstract

India has a diverse variety of medicinally important plants which have been claimed with beneficial therapeutic effects along with better tolerability in terms of side effects. *G. asiatica* also known as phalsa, a member of tiliaceae family is a small fruit crop cultivated in warmer season and is known to contain cyanidin 3- glucoside, vitamin C, minerals. A brief review of work so far carried out is compiled in the present study showing radioprotective, antioxidant, antimalarial, antihyperglycemic, antipyretic, analgesic, antifungal, antiviral, antiplatelet, anticancer and immunomodulatory effect of plant.

**Keywords:** *Grewia asiatica*, Traditional uses, Activity, Anthocyanins

### Introduction

*Grewia asiatica* belongs to family Tiliaceae. Plant of genus *Grewia* consists of shrubs and trees and majorly distributed in the warmer regions. Numerous species around 40 are found in India to name a few are *G. tenax*, *G. hirsuta*, *G. damine*, *G. Lasiodiscus*, *G. optiva*, *G. biloba*, *G. bicolor*, *G. tiliaefolia*, *G. flavescens* and many more. These species are the part of trade of medicinal and aromatic plants and are the income source particularly for the poor families. Plants belonging to this family are of enormous use economically and provide good source of naturally occurring fiber. Genus *Grewia*, yield only edible fruit of family Tiliaceae and that is only *Grewia asiatica*, the species of importance [Morton *et al.*, 1987] <sup>[1]</sup>. Phalsa (*Grewia asiatica*) is an exotic bush cultivated as a small fruit crop and also used as a folk medicine. Despite its diverse use, it has suffered disregard, as is seen from the meagre literature on this plant. As a step in this direction, we have reviewed the characteristics, phytochemistry and pharmacological properties of this plant. This article will serve as a useful piece of information for further research on this important plant.

### Other names/Synonyms

According to Sastri (1956) <sup>[2]</sup>, phalsa is the most commonly used vernacular name for these fruits in India but there are several names in customary usage including *parusha*, *dhamin* and *shukri* in Hindi, *dhaman* in Punjabi, *man-bijal* in Assamese, *mirgichara* and *pharasakoli* in Oriya, *phalsa* in Gujrati, *phalsa* and *shukri* in Bengali *phalsi* in Maharashtra, *jana*, *nallajana*, in Telagu, *buttiyudippe* and *tadasala* in Kannada, *palisa* and *tadachi* in Tamil and *falsa* in Pakistan.

### Origin and Geographical distribution

Phalsa plant is native to the Indian subcontinent and Southeast Asia and also distributed in the forests of central India, South India, Western Himalayas upto height of 3000 ft (Sastri *et al.*, 1956) <sup>[2]</sup>. It is cultivated commercially mainly in Punjab and around Bombay and in the semi-arid regions of Maharashtra, Gujarat, Rajasthan, Andhra Pradesh, Uttar Pradesh and Haryana.

### Morphology

Phalsa is a bush or average sized tree with long, slender, drooping branches, and the young branchlets are coated with hairs. Leaves which are widely spaced are heart-shaped or may be ovate, usually apex is pointed, base oblique, 8in in length and 6in in width and toothed coarsely. Flowers are yellow in colour and grown in cymes of 3-4, are 2 cm in diameter

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tomentose densely, ribbed. Fruit are lobed drupes [44]. The fruit changes colour from green to purple-red and after fully ripened to dark-purple. There are two kinds of fruits of phalsa, large fruits contains two hemispherical, tough, buff in colour seeds and small fruits contains single-seed. Phalsa is a self-pollinated crop usually. [Malik *et al.*, 2010] [3].

#### Microscopic Characters

*G. asiatica* shows presence of Prismatic and Rosette crystals, Parenchymal cells, Crystal fibre, Spiral vessels, Epidermal cells, Starch grains, Aleurone grains, Stellate hairs, which serve as an important microscopic diagnostic characters. [Joshi *et al.*, 2013] [4]



**Fig. 20:- Survey and collection of variability in *Grewia subinaequalis* (Phalsa)**

- (A) Natural wild population of phalsa trees in dry hilly tracks
- (B) Cultivation of phalsa in Pushkar, Rajasthan
- (C) Fruiting pattern of phalsa
- (D) Insynchronous maturity of phalsa fruits
- (E) Fully ripe fruits assembled for marketing
- (F) Fruit of two types being sold near Madar Gate in Ajmer, Rajasthan



**Fig a & b:** *G. asiatica* plant containing ripened and unripe fruits

### Traditional Uses

Use and cultivation of phalsa fruit has been mentioned in the ancient Indian literature and it has been used for various ailments in the Indian system of medicine. The unripe fruits are said to remove vata, kapha and biliousness. Root bark is used for treating rheumatism, fruit is used as astringent and stomachic and when unripe they alleviate inflammation and is used in respiratory, cardiac and blood disorders, and in fever [Morton *et al.*, 1987] <sup>[1]</sup>. Infusion of bark is given as demulcent, febrifuge, and for diarrhoea. The leaves are applied on skin eruptions and they are known to have antibiotic action.

### Economical uses

*G. asiatica* have enormous uses for economically weaker sections. Ripe phalsa fruits are eaten fresh and also made into soft drinks or squash during summer months in India. Fresh leaves of plant are used as animal fodder. The bark is used as

substitute of soap in Burma. Mucilaginous extract obtained from bark is used in clarifying sugar. Fiber obtained from the bark is used to make rope. <sup>[43]</sup>. Wood from plant is used for making archers' bows, shingles and poles for carrying of loads on the shoulders. [Yadav *et al.*, 1999] <sup>[5]</sup>

### Types

*G. asiatica* exists in two forms, i.e. tall and dwarf types of phalsa. Both forms are studied for differences in physical parameters, chemical constituents and electrophoretic patterns of seed proteins by SDS-PAGE. [Dhawan *et al.*, 1993] <sup>[6]</sup>

### Harvesting and Yield

Summer is the fruit bearing season for phalsa. Fruits perish in short time and so must be used for selling within 24 hours. Average yield per plant of phalsa is 9-11 kg in one season. (Morton *et al.*, 1987) <sup>[1]</sup>

**Table 1:** Nutrient content of phalsa fruits, [Yadav *et al.*, 1999] <sup>[5]</sup>

Nutrient Content	Nutrient in 100 g fruit
Calories (Kcal)	90.5
Calories from fat (Kcal)	0.0
Moisture (%)	76.3
Fat (g)	<0.1
Protein (g)	1.57
Carbohydrates (g)	21.1
Dietary Fiber (g)	5.53
Ash (g)	1.1
Calcium (mg)	136
phosphorus(mg)	24.2
Iron (mg)	1.08
Potassium (mg)	372
Sodium(mg)	17.3
Vitamin,B3, Niacin(mg)	0.825
Vitamin C (g)	4.385
Vitamin A (µg)	16.11
Vitamin B1(mg)	0.02
Vitamin B2(mg)	0.264

### Ash and Extractive Values

Total ash, acid insoluble ash and water- soluble ash values of fruit of *G. asiatica* are 3.0, 1.4 and 1.1% respectively. The ethanol soluble, methanol soluble, petroleum ether soluble, chloroform soluble, benzene soluble and ethyl acetate soluble extractives values are found to be 45.4, 46.2, 0.8, 1.6, 14.0 and 3.4%, respectively. [Gupta *et al.*, 2006] <sup>[7]</sup>

### Phytoconstituents of *Grewia asiatica*

Plant parts are found to have all the essential mineral elements, carbohydrates, proteins, fatty acids and other active metabolites like flavonoids, tannins, phenols, alkaloids, steroids and triterpenoids, lignans, lactones, flavones, anthocyanins etc. [Patil *et al.*, 2011, Ullah *et al.*, 2011] <sup>[8, 9]</sup>

*Grewia asiatica* contains anthocyanin type cyanidin 3-glucoside [10, Nair *et al.*, 2005] vitamin C, minerals and dietary fibers [Yadav *et al.*, 1999] [5]. GCMS Analysis of *Grewia asiatica* shows the presence of Citric acid trimethyl ester (5.10%), alpha.-methyl-1 sorboside (11.52%), stigmasterol (1.23%), campesterol (2.15%) and 9, 12-octadecadienoic acid, methyl ester (0.10%). [Gupta *et al.*, 2012] [11]. A new  $\delta$ -lactone i.e 3, 21, 24 trimethyl-5, 7-dihydroxyhentriacontanoic acid  $\delta$ -lactone is isolated from the flowers of *Grewia asiatica* [12, Lakshmi *et al.*, 1976]. The flowers contain grewinol (keto alcohol) and tetratricontane-22-ol-13-one. The seeds contain 5% of a bright-yellow oil containing 8.3% palmitic acid, 11.0% stearic acid, 13.4% oleic acid, 64.5% linoleic acid; 2.8% unsaponifiable [Morton *et al.*, 1987] [1]. In a study gas chromatography-mass spectrometry led to the identification of the principal component 2-(1-oxopropyl)-benzoic acid very similar to the active salt found in the standard drug Aspirin (2-acetyloxybenzoic acid) in Jwarhar Mahakashay ayurvedic preparation of which *Grewia asiatica* is a constituent. [Gupta *et al.*, 2010] [13]. Pigments and total soluble solids have been obtained from pomace.

Qualitative examination reveals the presence of Alkaloids, Sugars, Tannin & Phenolic compound, Steroids, Flavonoids. Drug is soluble both in water and alcohol, due to the respective soluble metabolites. [Joshi *et al.*, 2013] [4]

## Pharmacological activities

### Radio protective effect

A number of studies have been done to show protective effect of *Grewia asiatica* in radiation induced damages in different organs of rodents by a group of authors.

- In a study pretreatment with *Grewia asiatica* fruit pulp extract in Swiss albino mice protects hematopoietic system against radiation-induced damage. Radiation induced deficit in different blood constituents like glutathione, sugar and protein levels in serum is significantly increased, whereas increase in level of lipid peroxidation and cholesterol level due to radiation was markedly decreased in pretreated animals compared to control group. [Singh *et al.*, 2007] [14]
- Fruit pulp extract administered for 15 days at 700mg/kg shows radioprotective effect in swiss albino mice exposed to gamma radiation by decreasing enhanced lipid peroxidation and by checking the depleted level of glutathione and protein in cerebrum. [Ahaskar *et al.*, 2007] [15].
- Effect of *Grewia asiatica* extract as radioprotective agent is examined in testis. Histopathological study showed that due to radiation exposure spermatogonia "A", spermatogonia "B", spermatocytes and spermatid count declines significantly compared to the control group. Whereas these counts were higher in *Grewia asiatica* pre/post treated irradiated group compared to the respective radiation treated group. There is a significant depletion in testis weight after irradiation, whereas pre/post treated *Grewia asiatica* group showed significantly increase in values. [Sharma and Sisodia *et al.*, 2010] [16].
- *Grewia asiatica* shows hepatoprotective effect against oxidative stress induced by irradiation with gamma radiation by causing a significant elevation in liver DNA and RNA level in comparison to irradiated mice and increase in different hepatocytes counts thus protecting

liver against damages caused by radiation. [Sharma *et al.*, 2010] [17].

- Oral administration of 700 mg/kg of *Grewia asiatica* for 15 consecutive days before exposure to 10 Gy of radiation was found to afford maximum protection as mice of experimental group exhibited significant modulation of radiation- induced decrease of reduced glutathione (GSH) and radiation- induced increase in lipid peroxidation (LPO) in the whole brain and liver at 24 hours after radiation exposure. [Ahaskar *et al.*, 2007] [18]
- Supplementation of *Grewia asiatica* at 700mg/kg for 15 days prior to and post irradiation 5gy whole body radiation in mice ameliorated changes in the amount of cerebellar lipid peroxidation, Glutathione, protein, nucleic acids and histopathological changes significantly ( $p < 0.001$ ) showing its radioprotective as well as neuroprotective properties of extract against the radiation. [Sisodia *et al.*, 2009] [19]
- Administration of *Grewia asiatica* fruit extract to mice before and after irradiation caused a significant depletion in Thiobarbituric acid reactive substances content followed by a significant elevation in Glutathione and protein concentration in the intestine and testis of mice in comparison to irradiated mice. And it causes significant protection of DNA and RNA in testis. Extract also shows strong radical scavenging activity in 2, 2-diphenyl-1-picrylhydrazyl (DPPH) and O(2)(-) assays and also showed in vitro radioprotective activity in protein carbonyl assay showing its radio protective activity. [Sharma *et al.*, 2009] [20]
- In a similar studies administration of fruit pulp extract of *Grewia asiatica* to 5 Gy gamma radiation irradiated mice causes significantly amelioration of augmented lipid peroxidation and prevented significantly radiation induced depletion in the level of glutathione and protein in mice cerebrum. [Sisodia *et al.*, 2008, Ahaskar *et al.*, 2007] [21, 22]

### Anti-malarial and Antiemetic activity

- Crude alcoholic extract of *Grewia asiatica* possess antiemetic effect in experimental model dogs at a dose of 120mg/kg and control emesis induced by apomorphine at a dose of 0.44 mg/kg. Effect is significant in comparison to standard drug maxolon (metocloamide) and chlorpromazine or largactil. [Yaqeen *et al.*, 2008] [23]. In another study antimalarial and antiemetic activities of methanolic extract of leaves is assessed. The crude methanolic extract showed antimalarial activity, (69% inhibition), emetic action of methanolic extract was 39.14% and 59.69%, when administered to male chicks at 50 mg/kg and 100 mg/kg dose levels. [Haq *et al.*, 2012] [24]

### Antihyperglycemic activity

Various studies have been done on leaves, fruits, stem bark of *Grewia asiatica* to shows its antidiabetic activity.

- Alcoholic and chloroform extract of leaves of *Grewia asiatica* (200mg/kg) shows highest antidiabetic activity in alloxan induced diabetic wistar rats compared to control and glibenclamide (10mg/kg) when compared with bark of *Sesbania Sesban* and fruits of *Luffa acutangula*. [Patil *et al.*, 2010] [25]
- Different extracts of leaves of *Grewia asiatica* i.e

petroleum ether, ethanol and chloroform were tested for antihyperglycemic activity in alloxan induced diabetic rats. Ethanolic extract shows profound antihyperglycemic activity compared to control and glybenclamide. [Patil *et al.*, 2011] <sup>[8]</sup>.

- Comparative anti-hyperglycemic activity of ethanolic extracts of fruit, stem bark and leaves of *Grewia asiatica* and their fractions were examined in alloxan induced hyperglycemic rabbits. Crude extracts and their fractions i.e aqueous, methanolic, butanolic, ethylacetate, chloroform, carbon tetrachloride at the dose of 200mg/kg and 100mg /kg respectively reduced serum glucose level suggesting significant antidiabetic activity. [Abidah *et al.*, 2011] <sup>[26]</sup>
- Aqueous, methanolic and butanolic extracts of *Grewia asiatica* fruits were found to produce a stimulatory effect on ROS production however; the chloroform, hexane and ethanol-acetate extract exerted significant inhibitory effect. Hence *Grewia asiatica* fruit causes low glycaemic response and modulation of ROS production in healthy non diabetic humans. [Mesaik *et al.*, 2013] <sup>[27]</sup>.
- Administration of aqueous extracts of leaves orally (250 mg/kg and 500 mg/kg) to normal rats and streptozotocin (50 mg/kg) treated diabetic rats for 21 days significantly reduced blood glucose level in streptozotocin induced diabetic rats. Extracts significantly reduced the blood glucose level in a dose dependent manner as measured by oral glucose tolerance test. [Latif *et al.*, 2012] <sup>[28]</sup>
- In a study by Dogar *et al.* comparative evaluation of antihyperglycemic activity of three plants is done. Bark of *Grewia asiatica* reported highest significant reduction in glucose, cholesterol and triglycerides levels in blood in normal and alloxan diabetic rat, when compared with *Gossypium herbaceum* and *Gymnema sylvestre*. [Dogar *et al.*, 1988] <sup>[29]</sup>

#### Anti-platelet activity

- Crude methanolic extracts of leaves of *Grewia asiatica* exhibits potent platelet aggregation inhibition activity in a dose-dependent manner at concentration range (1 to 10 mg/ml) in arachidonic acid induced aggregation in human volunteers. Zial Ul haq *et al.*, 2012] <sup>[30]</sup>.

#### Analgesic and antipyretic activity

- Aqueous extract of fruits of *Grewia asiatica* possess antipyretic and analgesic activity at a dose of 200mg/kg and 300mg/kg. It shows good analgesic activity due to its inhibitory effect on pain induced by acetic acid writhing and tail immersion test. Extract at a dose of 400mg/kg had significant effect than aspirin, 100mg/kg on reducing pyrexia induced by administering lipopolysaccharides extract from *E.Coli*. [Das *et al.*, 2012] <sup>[31]</sup>
- Methanolic and aqueous extract of root bark of *Grewia asiatica* at a doses of 200mg/kg and 400mg/kg is subjected to Analgesic effect using acetic acid-induced writhing in mice and hot plate analgesia in rats and to anti-inflammatory activity using carrageenan-induced paw oedema. There is a significant inhibition by extracts on writhing response, increase in hot plate reaction time and also caused a decrease in paw oedema reflecting its analgesic and anti-inflammatory effect. [Paviaya *al*, 2014] <sup>[32]</sup>

#### Antioxidant activity

Medicinal plants typically contain mixtures of different chemical compounds that may act individually or in synergy to improve the health of common man. The majority of the antioxidant activity is due to the isoflavones, flavonoids, flavones, anthocyanins, lignans, coumarins, catechins and isocatechins which were shown to be present in *Grewia asiatica*. Antioxidant-based drug formulations are used for the prevention and treatment of complex diseases like Alzheimer's disease, stroke, cancer, diabetes and atherosclerosis etc which may arise due to oxidative damage by free radicals. [Kumar *et al.*, 2009] <sup>[33]</sup>. Anti-oxidant activity of *Grewia asiatica* have been studied by different authors.

- In a study by Siddiqi *et al.*, four polyphenolic fraction i.e Flavanols, flavonols, phenolic acids and anthocyanins of fruits of *G. asiatica*, *E. jambolana* and *C. carandas* is analyzed for total content of phenolics and flavanoids as well as for antioxidant activity by  $\beta$ -carotene-linoleic acid assay, DPPH and total reducing power assay. Maximum antioxidant activity is found in DPPH assay, 62-85% and  $\beta$ -carotene-linoleic acid assay it is found to be 58-89. DPPH scavenging activity of flavanol fraction in *G. asiatica* (85% at 20 ppm) was comparable to BHA (89%). [Siddiqi *et al.*, 2013] <sup>[34]</sup>
- In another study comparison of Quercetin and total flavanoid content as well as antioxidant activity of in vitro and in vivo parts of *Grewia asiatica* is done. The flavanoid contents in the in vivo (leaf, stem) and in vitro (old callus) plant parts were found to be present in the alcoholic, chloroform and aqueous solvents. Amount of Quercetin in the leaf sample was found to be double that of the callus (4.28ng/ $\mu$ l). Antioxidant potential of fruit extract was observed maximum (98.2%) among all plant parts. For the stem extract it was found to be higher (89.8%) than leaf and callus by the DPPH assay. Thus showing presence of flavonoids and enormous antioxidant activity of lant [Sharma *et al.*, 2013] <sup>[35]</sup>
- The successive extracts of *Grewia asiatica* exhibited antioxidant activity in the DPPH and the nitric oxide radical inhibition assay as evidenced by the low IC 50 values. The successive extracts such as petroleum ether, benzene, ethyl acetate, methyl alcohol, water and 50% crude methanolic extracts exhibited IC 50 values of  $249.60 \pm 7.37$ ,  $16.19 \pm 2.132$ ,  $26.17 \pm 1.49$ ,  $27.38 \pm 1.80$ ,  $176.14 \pm 5.53$  and  $56.40 \pm 3.98$   $\mu$ g/mL, respectively in DPPH and  $22.12 \pm 02.65$ ,  $27.00 \pm 01.62$ ,  $47.38 \pm 05.88$ ,  $56.85 \pm 06.16$ ,  $152.75 \pm 5.76$  and  $72.75 \pm 13.76$   $\mu$ g/mL, respectively in nitric oxide radical inhibition assays. These values are more than those obtained for ascorbic acid and quercetin as standards. [Gupta *et al.*, 2007] <sup>[36]</sup>

#### Antifungal and Antiviral activity

- In a study by Kumari *et al.*, it was found from the MIC studies of methanolic extract of leaves of *Grewia asiatica* that the sensitivity pattern of the organism was found to be decreased in the order: *Candida albicans* than *Aspergillus thioogenitalis* then *Penicillium notatum*, *Penicillium citrinum* and *Aspergillus niger*. So, it was found that it was active maximum against *Candida albicans*. However, *Aspergillus niger* was totally resistant against the extract. The examination of antiviral potency of the extract showed the maximum inhibitory

property at a concentration of 1000g/ml against Urdbean leaf crinkle virus. [37, Kumari *et al.*, 2009] <sup>[37]</sup>

### Anticancer activity

As there is vast range of antioxidants in *G. asiatica* like vitamin c, anthocyanins, carotenoids etc, anti-tumour activity has been studied by various authors which shows role of plant in anticancer activity.

- Marya *et al.* determined in-vitro cytotoxic activity of aqueous extract of fruits and leaves of *Grewia asiatica* by MTT assay using cell lines HEK-293 (Epidermal Kidney Cancer cell line), NCI-H522 (Cell Lung cancer cell line), HELA (Cervical Cancer cell line), Hep – 2 (Laryngeal Cancer cell line), and MCF-7 (Breast cancer cell line). From the results it is concluded that the aqueous extracts of leaves and fruits showed significant activity against liver cancer and breast cancer. [Marya *et al.*, 2011] <sup>[38]</sup>
- In another study in vitro cytotoxic activity of methanolic extract of fruit of *Grewia asiatica* is determined by MTT Assay using cell lines HEK-293 (Epidermal Kidney Cancer cell line), NCI-H522 (Cell Lung cancer cell line), HELA (Cervical Cancer cell line), Hep – 2 (Laryngeal Cancer cell line), and MCF-7 (Breast cancer cell line). Comparable cytotoxicity was found against lung cancer cell line and breast cancer cell line respectively but no activity found against normal cell line, Cervical cancer cell line and Larynx cancer cell line. [Dattani *et al.*, 2011] <sup>[39]</sup>
- Methanolic extract of *Grewia asiatica* when administered at 250 and 500 mg/kg ip showed anticancer activity against Ehrlich's ascites carcinoma (EAC) cell lines and increased the life span of EAC ascitic tumor bearing mice by 41.22% and 61.06%, respectively. Extract was assessed for in-vitro cytotoxicity activity against four cancer cell lines and showed 50% cytotoxicity at 53.70, 54.90, 199.5 and 177.8 µg/ml, for HL – 60, K-562, MCF-7 and Hela cells respectively. [Kakoti *et al.*, 2011] <sup>[40]</sup>
- In a study crude ethanolic extract and fractions of fruit, stem bark and leaves of *Grewia asiatica* are subjected to cytotoxic assay using brine shrimps and investigated for hemagglutination activity. Hemagglutination activity is used to determine effect of drug on blood and determines safety margins in case of blood disorders like haemorrhages and clot formation. It was concluded that *Grewia asiatica* have insignificant brine shrimp lethality and hemagglutination activity was found to be absent. [41, Abidah *et al.*, 2013]

### Immunomodulatory effect

- Many indigenous medicinal plants have been reported to possess immunomodulatory effect by improving defence mechanism of the body also known as rasayanas. In a study Ethanolic extract of fruit of *Grewia asiatica* at 200 and 400 mg/kg showed significant immunostimulant property. It counteracts effect of cyclophosphamide-induced reduction in total WBC, % neutrophil and haemoglobin levels and showed increase in the phagocytic index in assay of carbon clearance [42, Singh *et al.*, 2014] <sup>[42]</sup>

### Conclusion

The global scenario is changing their face towards herbal medicinal uses due to less side effect and emphasis given to

develop a modern drug to cure many acute diseases. *Grewia asiatica* is the plant which may not be freely available in future due to overexploitation, habitat destruction or lack of domestication and cultivation. Therefore this review served as an important reference for reviewing and timely recognition of enormous medicinal application of this plant.

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