International Journal of Emerging Trends in Science and Technology
IC Value: 76.89 (Index Copernicus) Impact Factor: 4.219 DOI: https://dx.doi.org/10.18535/ijetst/v4i9.15

Grewia (Malvaceae *sensu lato*): ethnomedicinal uses and future potential

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Abstract
Knowledge of traditional uses of plants or plant based products among the folks or various communities around the world had been the primary key for many scientific exploration of drug discovery. The plants of pharmaceutical or medicinal importance are under pressure because of demand and over exploitation. The current review presents the potential of *Grewia*, a genera of family Malvaceae *sensu lato* as an alternative source for the commercialization of G*rewia* species based plant products for various purpose. Traditionally *Grewia* species were used for the treatment of many disease such as Malaria, Tuberculosis, Syphilis, Fever etc. *Grewia* species exhibited low cytotoxic properties. Ethnomedicinally, two species of *Grewia* i.e. *G. asiatica* and *G. mollis* had been used widely in African and Asian countries and exhibits future potential for commercialization.
Keywords: Ethnomedicine, *Grewia*, Malaria, Malvaceae *sensu lato*, Syphilis, Tuberculosis.

1. Introduction

Since the dawn of human race ethnomedicinal plants have been the source of various remedies. Most of the significant drug discoveries in past were based on the traditional knowledge present amongst the folks of various parts of the world. At present there are numerous research programs running worldwide to utilize the plants mentioned in the traditional documents such as Ayurveda. The plants listed in traditional documents are used widely either as medicines or as food supplements. The demand of plants of importance has created the pressure on such groups. The over exploitation of natural resources in terms of biodiversity has to be curbed and need of alternative plant resources is the current demand. As an alternative, *Grewia*, a genera of family Malvaceae *sensu lato*, presents an option before us, because it has various ethnomedicinal properties and used widely amongst the developing and under developed countries. The current review summarizes the ethnomedicinal properties of *Grewia* plants and its potential in near future.

2. Systematic Position and External Morphology

Grewia, a genera of Family: Malvaceae *sensu lato* (according to Angiosperm Phylogeny Group (APGIV) Website), was placed earlier in Family: Tiliaceae, Series: Holopetalae, Tribe: Grewieae (Hooker, 1875). According to the plant list there are 325 accepted species name of *Grewia*, all around the globe. Morphological characters of *Grewia* are: Trees or shrubs; Leaves entire, one to nine nerved; Flowers mostly axillary and some members are panicled; Aposepalous; Petals five in numbers with glands present at the base, sometimes absent; Stamens numerous on a raised torus; Staminodes absent; Syncarpous; Ovary superior present on top of androphore; Placentation axile; Fruits Drupe.

3. Traditional Importance

In Ethopia, decorated sticks known as Napala is made up of *G. bicolor* and was used by the elderly peoples whereas *G. kakothamnos* was used in making bow known as Omo (Teklehaymanot and Giday, 2010). *G. micrantha* Boj, stems and branches were used in making handicrafts in Mozambique (Bruschi et al., 2014). In Kenya, *G. similes* and *G. tembensis* used for construction purpose (Bussmann et al., 2006). *G. retinervis*

Burret stems and branches were used as firewood in South Africa (Rasethe et al., 2013).

4. Edible species

Fruits of *G. optiva*, *G. asiatica* (Hindi: Phalsa), *G. pachycalyx* and *G. bicolor* Juss. var. *bicolor* were eaten in Nepal, India, Mozambique and South Africa respectively (Uprety et al., 2012; Rasethe et al., 2013; Bruschi et al., 2014). *G. avellana*, *G. flavescens* and *G. schinzii* fruits were used in making beer and generate income in Namibia whereas *G. villosa* leaves are used in the brewing of beer in Kenya (Kipkore et al., 2014; Cheikhyoussef and Embashu, 2013). *G. mollis* Juss. flowers, fruits and leaves were used as vegetables and condiment in Benin (Segnon and Achigan-Dako, 2014). *G. lasiodiscus* fruits were used as condiment in Benin (Segnon and Achigan-Dako, 2014). *G. tenax* and *G. villosa* were used as fodder and fruits were consumed by the natives of North-West Pakistan (Ahmad and Pieroni, 2016). *G. bicolor* and *G. tembensis* ripe fruits eaten by women and children (Bussmann et al., 2006). *G. similis*, *G. bicolor* and *G. tembensis* were used as fodder for domestic animals in Uganda and Kenya (Bussmann et al., 2006; Nampanzira et al., 2015).

5. Ethnomedicinal properties

a. Antivenom

In Kenya, leaves of *Grewia* sp. were crushed and were used to wipe the snake bitten area of livestocks' (Owuor and Kisangau, 2006).

b. Oral Hygiene

G. similes, *G. tembensis* and *G. bicolor* used as toothbrush as dental hygiene and bad breath (Bussmann et al., 2006; Belayneh and Bussa, 2014; Kipkore et al., 2014).

c. Veterinary disease treatment

G. mollis bark was crushed and homogenized in water and administered orally used for constipation in livestocks (cattle) (Bekalo et al., 2009). *G. villosa* administered orally to camels suffering from delayed placenta disease (Giday and Teklehaymanot, 2013). *G. flavescens* Juss. var. *flavescens* roots and leaves used in Cattle retained placentia (Cheikhyoussef and Embashu, 2013). Bark of *G. bicolor* was grinded and mixed in water and salt added finally given for the cattle which placenta is delayed during delivery (Megersa et al., 2013).

d. Human disease treatment

In Ethopia, fruits of *G. bicolor* soaked in water was used in the treatment of Veneral disease/Syphilis whereas leaves, laxative and bark were used in the intestinal infection and stomach disorders ; decoction prepared from the roots of *G. kakothamnos* was used in the treatement of respiratory infection and tuberculosis; concoction prepared from the fruits and roots of *G. ferruginea* was administered orally by the patients suffering from kidney infection and intestinal parasites (Teklehaymanot and Giday, 2010; Belayneh et al., 2012). In Mozambique, *G. monticola* Sond. fruits were heated and grinded and applied topically in ear treatments; fruits and seeds were heated and grinded and used topically in wounds; stems were heated and grinded and used topically in swellings; and decoction prepared from the roots were administered orally in diarrhea (Ribeiro et al., 2010). Crushed or infusion of bark of *G. villosa* was used in abscess and swelling (Teklehaymanot and Giday, 2010).

Some *Grewia* sp. used in stomach related disorders in African continent are *G. flavescens* (leaves were used in stomach disorders), *G. bicolor* Juss. (root extracts drunk as diarrhoea and gonorrhoea), *G. flavescens* Juss. (leaves are used in cough whereas roots extract drunk in diarrhea menorrhagia), *Grewia avellana* Hiern (roots are used in diarrhoea) and *Grewia schinzii* K. Schum. (fruits were used in heartburn) (Cheikhyoussef and Embashu, 2013; Maroyi, 2011; Ribeiro et al., 2010).

In West Ethopia, *G. ferruginea* leaves were used in washing hairs and used as a soap against Dandruff (Megersa et al., 2013). *G. bicolor* leaves are crushed and bandage of it was applied on small swelling with oozing pus/skin ulcer whereas extracts of leaves were used in epidermal drying as emollients (Belayneh and Bussa, 2014). In Australia, root and bark of *G. mesomischa* was used in stomach ache (Deo et al., 2016). *G. tenax* is used in liver disorders, jaundice, and inflammatory condition (Sharma and Patni, 2012; Safa et al., 2012; Al-Said et al., 2011). *G. mollis* was used in liver disease, abdominal problems, arthritis, and inflammatory conditions (Al-Youssef et al., 2012; Asuku et al., 2012; Al-Asmari et al., 2014). *G. erythraea* Schweinf. leaf and stem were used as diuretic and haemostatic and for kidney diseases (Al-Musayeib et al., 2012). *G. carpinifolia*, *G. elastic*, *G. umbellifera*, *G. tenax* and *G. tiliaefolia* ethanolic extracts improves muscular strength and possess Central Nervous System (CNS) depressant activity and used traditionally to manage various CNS

disorders (Olamide et al., 2016; Pfau and Skog, 2004). *G. bicolor* roots were used as tranquilizer (Shamoun et al., 2014). Amongst all *G. bicolor* species is used frequently in various parts of the world for the treatment of many diseases. Roots extracts of *G. asiatica* (Sanskrit: Parushak) is used in the polyherbal Ayurvedic preparation i.e. *Jwarhar mahakashay* and used traditionally as antipyretic (Gupta et al., 2010).

g. Antimalarial

Ethnomedicinally, decoction prepared from the leaves of *G. hainesiana* and roots of *G. trichocarpa* were administered orally for the treatment of Malaria by the Digo community of Kenyan Coast (Nguta et al., 2011).

6. Physicochemical compositions

Grewia sp. produces various classes of compounds such as flavones, triterpenoids, sterols, gulcosides, alkanol, polyphenols and carbohydrates. *G. mollis* extract exhibited the presence of various compounds such as Luteolin, tetrahydroxyflavone, 7β-hydroxy-23-enedeoxojessic acid, 7β-hydroxy-23-deoxojessic acid, β-sitosterol, and β-sitosterol-3-o-glucoside (Al-Youssef et al., 2012; Asuku et al., 2012; Al-Asmari et al., 2014). *G. tenax* extract chemical composition was reported and confirmed the presence of Betulin, triacontan-1-ol, α-amyrin, β-amyrin, β-sitosterol, lupenne, erythrodiol, and tetratriacont-21-ol-12-one (Sharma and Patni, 2012; Safa et al., 2012; Al-Said et al., 2011). *G. asiatica* produces polyphenolic compounds (Siddiqi et al., 2011).

7. Grewia gums

Glucose, rhamnose, galactose, arabinose and xylose were the main monosaccharide components whereas galacturonic acid was the main sugar acid (Nep and Conway, 2011; Okafor et al., 2001). Grewia gum is polymeric in nature and have the potential to be used in various process viz. film coating agent, suspending agent and as mucoadhesive, but due to low solubility in aqueous solvent system grewia gum has limited commercial applications whereas study performed on different fractions of grewia gum had exhibited better thermal stability and possibility of commercialization (Oqaji et al., 2013). Martin et al., (2008) had assessed the binding and compressional property of grewia gum and compared it with the polyvinylpyrrolidon (PVP) and exhibited that grewia gum had higher degree of packing and improved fluidity granules than PVP. Grewia gum obtained from inner stem bark of *G. mollis* can be used as a suspending agent in oral formulations (Ogaji and Hoag, 2011). Nap and Conway (2010) performed the experiments on the matrix based tablets of grewia gum and cimetidine and found out that grewia gum can control the cimetidine drug release up to 12 hours and showed the importance of grewia gum in controlled drug release. Ogaji and Okafor (2011) exhibited that grewia gum coated tablets of praziquantel exhibits increase in disintegration time, thus have the potential to be used as a coating agent.

8. Antiprotozoal property

Al-Musayeib et al., (2012) evaluated the methanolic extract of *G. erythraea* against *Plasmodium falciparum, Leishmania infantum, Trypanosoma cruzi* and *T. brucei*. The antiprotozoal activity in terms of 50% Inhibitory Concentration were found to be 11.7±3.5, 24.1±3.8, 8.2±1.8 and 2.6±0.9 µg/ml respectively for aforementioned protozoans.

9. Cytotoxicity

Methanolic extract of *G. erythraeae* on fibroblast (MRC-5 SV2) cell line exhibited LC_{50} =27.2 ± 6.1 µg/ml (Al-Musayeib et al., 2012). Cytotoxicity of ethanolic extract of bark of *G. paniculata*, evaluated via brine shrimp lethality bioassay, exhibited LC_{50}=3.01µg/ml compared to vincristine sulphate (anticancerous drug) LC_{50}=0.52µg/ml (Nasrin et al., 2015). *G. mollis* bark and leaves extract was evaluated for the cytotoxic effects and found out that the permissible limit for safe consumption was 1500 mg/Kg of body weight for humans but the cautions has to be taken in case of patients suffering from renal failures (Onwuliri et al., 2006).

10. Miscellaneous

G. asiatica bark and fruits extracts possessed antidiabetic property, ability to restore glycogen, prevents pancreatic oxidative damage, inhibition of γ-radiation-induced glutathione depletion and ameliorating lipid peroxidation levels, inhibition of writhing and decrease in paw oedema and antihyperglycemic activity (Khatune et al., 2016; Khattab et al., 2015; Paviaya et al., 2013; Sharma and Sisodia, 2009; Sisodia et al.,2008). (4Z, 12Z)-cyclopentadeca-4,12-dienone isolated from the methanolic leaf extract of *G. hirsuta* exhibits antidiabetic potential in *In silico* study (Natarajan et al., 2015). Sana et al., (2015) has synthesized

spherical silver nanoparticles (50-70nm) from the leaf extract of *G. flaviscences*.

11. Conclusion

Grewia species posses various compounds such as carbohydrates, glucosides, polyphenols, triterpenes and sterol compounds which are responsible for various ethnomedicinal properties. Some of the properties were scientifically evaluated viz. antihyperglycemic activity, pancreatic oxidative damage and many more. Among all species *G. mollis* and *G. asiatica* are the two species which were used extensively for ethnomedicinal purpose by the folks of African and Asian subcontinent.

Acknowledgements

Thanks are due to Head, Department of Botany and Principal, SS Khanna Girls' Degree College, Allahabad, U.P., India for the facilities provided.

Conflict of Interest: The author do not have conflict of interest.

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