



PHARMACOLOGICAL AND PHYTOCHEMICAL PROPERTIES OF KAITHA (*FERONIA LIMONIA* L.) : A REVIEW

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Abstract

India is a rich source of many underutilized medicinal plants that possess the potential to treat diverse human ailments and diseases. Among them, kaitha is an indigenous plant of India which has been used in the folk medicine of the Indian traditional system since prehistoric times. Kaitha belongs to the family Rutaceae and one of the important plant with several medicinal and nutraceutical properties. Recently, extensively scientific studies have validated its ethnomedicinal properties and a variety of bioactive compounds in different parts of kaitha. The leaves, bark, roots, fruits and seeds are used extensively in Ayurvedic medicine and also commonly used in the treatment of chronic diarrhea, dysentery, and peptic ulcers, as a laxative and to treat myriad ailments. Although, its fruits are most commonly used for food products as murabba, puddings and fresh juice but the fruit pulp possesses broad range of therapeutic effects also which includes free radical scavenging, antioxidant, inhibition of lipid peroxidation, antibacterial, antiviral, anti-diarrheal, gastro-protective, anti-ulcerative colitis, hepatoprotective, antidiabetic, cardioprotective and radioprotective effects. This review summarizes the morphology, nutritional values, phytochemistry and therapeutic activities of the kaitha fruit that has been largely underutilized and neglected.

Key words: Kaitha, Ayurvedic medicine, Phytochemistry, Nutraceutical properties, Therapeutic activities

Introduction

Since prehistoric times, medicinal plants have been used in traditional health care. Medicinal plants are the plants that have therapeutic activities such as anti-diabetic, anti-cancer, anti-microbial, anti-bacterial and lipid lowering due to the presence of several secondary metabolites such as carotenoids, flavonoids, polyphenols, lignins, alkaloids and terpenoids. These are diverse group of compounds that are not essential for growth however, play important role in stress condition in order to survive and prevent molecular damage. In ancient time, people knew their medicinal values by their personal experience however, were not understand the scientific rational and working of their medicines. Now, we are in better position to understand the physiology and therapeutic doses of plants as multifunctional chemical entities for the treatment of chronic and acute disease. Medicinal plants are widely used in non-industrialized societies, mainly because they are economical, readily available and lesser side effects than modern medicines (Malviya *et al.*, 2012). India is known as “Botanical garden” having 17000 higher plant species of which 7500 are known as

medicinal plants (Shiva *et al.*, 1996). It has always been a platform for traditional medicinal system as Ayurveda, Unani, Sidha and local health traditions for treating various kinds of diseases. India is the leading country having lot of medicinal plants such as bael, jamun, karonda, passion fruit, phalsa, pomegranate, pumpkin, tamarind that have been used to prevent and treatment of diseases.

Among them, kaitha had traditionally been used in many herbal remedies such as digestive, stimulant, carminative, astringent and as an anti-diarrheal over the thousand years. It is the native of India and commonly known as wood apple, elephant apple, monkey fruit or curd fruit (English), Belada/Byalada Hannu (Kannada), Vellaga Pandu (Telgue), Vilam Palam (Tamil), Vilam Kai (Malayalam), Kaitha or kath bael (Hindi), Kavath (Marathi) and Kapittha, Dadhistha, Kapipriya, Dadhi, Puspaphala (Sanskrit). It is cheap, highly nutritious and seasonally available fruit that can be preserved for human consumption throughout the year. Ethanopharmacological properties of different part of wood apple plant have been documented in various studies (Pandey *et al.*, 2014) however still these are

underutilized. Limited studies on therapeutic and pharmacological activities of kaitha have been reported. Keeping this in view, the present review study aims to document the nutritional and ethnomedicinal properties of kaitha to encourage the use of these medicinal plants as potential source of drugs throughout the world.

Morphology

It is native to India, Pakistan, China and other Southeast Asia. It is deciduous, slow-growing, erect tree with slender branches having rough and spiny bark, approximately 9 meter in height. Tree grows in a monsoon climate with distinct dry season up to an elevation of 450 meter is capable to tolerate drought and best adopted to light soils. Leaves contain 5-7 leaflets which are 25-30 millimetres long and 10-20 millimetres broad. Leaves provide citrus-scent when crushed. Flowers (1.25 centimetres) are bisexual, dull red or greenish in colour having lateral panicles. Flowering occurs in February and March. It has a spherical fruit with 5-12.5 cm diameter that has outer woody hard shell called as rind. It is grayish-white in color and 6 mm thick which is very difficult to crack open. Hammer is used to crack the hard rind of wood-apple fruit. The Pulp of fruit is brown, aromatic, resinous, sour or sweet with many small white seeds embedded in it. Fruit matures in October and November. In India, the fruit ripens from early October through March (Rathnayake, 2006). It is consumed in the form of syrups, drinks, jellies and jams which can be prepared from its sticky pulp. Four species of kaitha are known namely *Feronia limonia* Swingle (f.l.), *Feronia elephantum* Correa (f.e.), *Limonia acidissima* L.(l.a), *Schinus limonia* L.(S.C.)

Taxonomy

Kingdom	:	Plantae
Sub-kingdom	:	Tracheobionta
Superdivision	:	Spermatophyta
Division	:	Magnoliophyta
Class	:	Magnoliopsida
Subclass	:	Rosidae
Order	:	Sapindales
Family	:	Rutaceae
Genus	:	Limonia L.
Species	:	Acidissima.

Nutritional Composition

Physicochemical studies have revealed that kaitha is rich in several nutrients such as water, pectin, fibers, calcium, vitamin B and vitamin C. Kaitha contains 28% protein. The concentrations of leucine, isoleucine, phenylalanine, tryptophan, valine and threonine were found to be present in higher amount in fruit and seed (Ramakrishna *et al.*, 1979, Deivamarvdhachalam *et al.*,

2013& Rao *et al.*, 2011). In traditional medicine, it has been used for treatment of diarrhoea and dysentery due to its high content of fiber that have beneficial effects related to digestibility in the small intestine (Bhatt and Jha 2015). Kaitha fruit, leaves and seed contain essential oil (Kumar *et al.*, 2010). Fruit oil is yellow with an iodine value 131, saponification value 192 and unsaponification matter 1%. Fatty acid profile of fruit reveals presence of various fatty acids such as palmitic acid, stearic acid, oleic acid, linoleic acid and linolenic acid while unripe fruit contains stigmsterol (Kumar *et al.*, 2010, Rathnayake, 2006 and Intekhab *et al.*, 2009). It contains low amount of fat which is ideally required for weight management and rich in high density lipoprotein (HDL) well known for cholesterol lowering activity thus may reduce the risk of heart diseases (Kumar *et al.*, 2010). Kaitha pulp is rich in several mineral such as calcium, phosphorus, iron, zinc. Calcium is crucially required for the rigidity of the skeleton and neuromuscular functions, blood clotting and many other metabolic processes. Phosphorus plays an important role in bone formation along with other metabolic activities of the body. Iron is used to prevent against anaemia, tuberculosis and disorders of growth as well as zinc have antioxidant potential which improve the diabetic symptom. The pulp is rich in vitamins such as beta -carotene, which is a precursor of vitamin A (Khare *et al.*, 2018). It helps to build and maintain teeth, bones and mucous membrane. It contain appreciable amount of gamma-tocopherol that shows anticancer, anti-inflammatory and cardio protective effects. Thiamine and riboflavin respectively helps into conversion of carbohydrate into energy and these are essential for growth, production of red blood cells and healthy skin and eye. Pulp also contains maltol, a flavour enhancer and isosorbide which is used to treats chest pain (Pandey *et al.*, 2014). Physico-chemical changes during maturation of kaitha is observed as total soluble solid (TSS), TSS: acid ratio, reducing, non reducing and total sugar increased as fruit ripened while total phenolic content (TPC), pectin content, ascorbic acid and pH is decreased during growth and development of fruit (Kumar *et al.*, 2017 and Sharma *et al.*, 2014) Table 1 depicts the proximate composition of kaitha.

Kaitha pulp has antioxidant and electron donor property for eight enzymes in humans. Its antioxidant property effectively ameliorated and altered the biochemical markers. Antioxidant property could be attributed to phenolic compounds, phenolic glycosides and flavonoid which possess antimutagenic and antibacterial activity. It decrease the level of tryptophan aminotransferase of Arabidopsis (TAA), glutathione (GSH) and also the activity of catalase (CAT),

superoxide dismutase (SOD) and glutathione peroxidase (GPX) which is used as nutritional supplement and protects against hepatic and renal oxidative stress. It contains tannins, coumarin, flavonoid and essential oil (terpenoid) in appreciable amount. Marmesin, a furanocoumarin and luteolin determines its antioxidant activity.

Phytochemical Composition

Kaitha have good nutritional and medicinal values. Different extract of kaitha reported to possess wide bioactive compounds such as phenols, flavonoid, alkaloids, terpenoids, tannins, saponins, fat steroids, glycosides, gum mucilage and fixed oil. Since Vedic times, the different parts of the plant include its roots, fruits, bark and the leaves have been used for various therapeutic purposes such as diarrhea, dysentery, as cardiac and liver tonic.

Leaves of the kaitha reveal the presence of various phytochemical compounds. Recently, preliminary phytochemical analysis of leaves shows the different chemical groups such as polyphenols, flavonoid, (imperatorin, bergapten and xanthotoxin), alkaloid, steroid and amino compounds which possess antimicrobial, anti-inflammatory, diuretic, antiasthma, and analgesic potential. Essential oil of kaitha shows prevention of deoxyribose degradation, cytotoxicity and DNA fragmentation activity against breast cancer cell (Kumar *et al.*, 2009). Seeds of kaitha contain several phytochemical compounds such as psoralen, bergapten, orientin, vitexin and saponarin which are used in the treatment of many diseases such as diarrhoea, urinary disorders, treatment of piles or haemorrhoids, acidity, ulcers, ringworm and other chronic skin infections (Intekhab *et al.*, 2009). Although it also contains anti-nutrients such as tannin, saponins, oxalate and phytate that interfere in absorption and metabolism of many nutrients such as amino acid, vitamins and minerals (Bhanupriya *et al.*, 2016).

Bark extract of kaitha contains phenol, nitrogen compound, vitamin compounds which possess antioxidant, antimicrobial, anti-inflammatory, colour pigment, diuretics, antiasthmatic activity (Muthulakshmi *et al.*, 2012). The stem barks of kaitha reported to contain flavanone, alkaloid, coumarin, lignin, sterol and triterpene and shown cytotoxic and antioxidant activity (Intekhab *et al.*, 2009, Shermin *et al.*, 2012). Root bark of kaitha also contains osthol, geranyl, umbelliferone, marmin, marmesin, aurapten, bergapten, isopimpinellin and peronoil. Marmesin, identified in the bark of kaitha which is most prevalent linear dihydrofuranocoumarin, belongs to the families of umbelliferae had been shows anti-tumor, larvicidal and antimicrobial activity (Jain *et al.*, 2010). Table 2 depicts

the phytochemical composition of kaitha in different solvent extract and Table 3 shows the physicochemical analysis of kaitha leaves.

Pharmacological Activities of Kaitha

(a) Anti-diabetic effect

Diabetes mellitus (DM) is a metabolic syndrome characterised by hyperglycaemia and other late complications such as retinopathy, nephropathy. Due to its fatal complications, DM is the seventh leading cause to death in the human society. Kaitha pulp extract showed significant decrease in blood glucose level, possess marked degranulation in beta-cells of pancreas by stimulating insulin secretagogue activity (Gupta *et al.*, 2009). The pulp shows significant potential of the insulin effect of plasma through increasing either the pancreatic secretion of insulin from beta cell of the islets of langerhan's or its release from the bound form (Mishra *et al.*, 2011). Along with significant decrease in blood glucose level it also lowers serum cholesterol level and helps regain in body weight of diabetic rats (Priya *et al.*, 2011). The aqueous fruit extract exhibited significant hypoglycaemic effect in hyperglycaemic rat (Kangralkar *et al.*, 2010). The pulp extract significantly decrease the level of MDA and increase the level of antioxidant enzymes such as SOD, CAT in blood serum of diabetic animals (Ilango and Chitra, 2009).

(b) Anti-hyperlipidemic activity

Hyperlipidemia is a major risk factor for atherosclerosis that is associated with oxidative stress. Hyperlipidemia, oxidative stress and atherosclerosis, all three are among the most important risk factors for cardiovascular diseases. Oral administration of methanol extract of kaitha leaves have lipid lowering activity and reported to have significant role in reduction of serum lipid parameters such as total cholesterol, triglyceride, low density lipoprotein, very low density protein and elevation in high density lipoprotein and faecal fat content (Pandit *et al.*, 2014).

(c) Anti-cancer and hepatoprotective activity

Cancer is a group of diseases which involve abnormal cell growth with the potential to invade or spread to other parts of the body. The signs and symptoms include a lump, abnormal bleeding, prolonged cough along with unexplained weight loss and a change in bowel movements. Liver plays a major role in various stages of biochemical and physiological activities such as energy and nutrient supply, homeostasis, immunity, detoxification as well as metabolism and storage of nutrients (Singh *et al.*, 2016). Hepatocellular carcinoma is one of the most commonly detected cancers. Luteolin, isolated from kaitha pulp shows anticancer activity in human hepatocellular

carcinoma cell line by cytotoxic and apoptotic activity (Jayshree *et al.*, 2014). Ethyle acetic extract of pulp possess cytotoxic activity. Kaitha leaves extract shows hepatoprotective potential by monitoring activity levels of serum glutamate oxaloacetic transaminase (SGOT) & serum glutamate pyruvic transaminase (SGPT). Activity level of aspartate aminotranferase(AST) and alanine aminotransferase (ALT) and cell viability in HepG2 cell improved after the supplementation of bark extract or fractions along with this pre-supplementation of bark methanol extract significantly prevented hepatic damage and depletion of cellular antioxidant and showed minimal distortion in the histoarchitecture of liver (Jain *et al.*, 2014). It is significantly lowered the mortality rate and showed improvement in liver function parameters in diabetic rats without change in liver weight, volume and serum glucose levels shows promising activity against liver necrosis in diabetic rats and so might be useful for prevention of liver complications in diabetes mellitus (Sharma *et al.*, 2012).

(d) Anti-bacterial Activity

Pathogenic microorganisms are becoming a major cause of morbidity and mortality in immune compromised patients. Microorganisms like bacteria tend to become resistant to drugs, coupled to the importunate side effects of some antibiotics. Many infections due to microorganisms lead to the production of strongly reactive molecules from the oxygen metabolism that can give rise to a variety of pathological conditions such as atherosclerosis, cardiovascular dysfunction, inflammation, carcinogenesis, reperfusion injury, drug toxicity and neurodegenerative diseases. There is a vital need to control microbial infections using appropriate antimicrobials devoid of side effects (Nateng *et al.*, 2017). Ethanolic extract of kaitha leaves reveals antibacterial activity against *shigella boydii*, *shigella dysentery* and *shigella flexnerii* and shows the reduction in severity and frequency of diarrhoea (Bellah *et al.*, 2015) The essential oil of leaf contained 14 compounds representing 98.4% of the total oil screened for its antibacterial activity against different clinically isolated gram+ and gram- strains (Kumar *et al.*, 2010). Antibacterial activity was evaluated for 4 bacterial strains including 2 gram+ such as *Staphylococcus aureus*, *Streptococcus faecalis* and 2 gram- such as *Pseudomonas aeruginosa*, *Escherichia coli*, all four strains showed muscle relaxant and antibacterial activity (Praveen *et al.*, 2015).

(e) Anti-fertility Activity

Wood apple pulp markedly reduced the epididymal and testicular protein content as well as glucose -6-phosphate dehydrogenase and Δ^5 -3 β -hydroxy steroid dehydrogenase level which improve sperm count,

motility, viability and decrease % of abnormal sperm, while a significant elevation was observed in testicular cholesterol and ascorbic acid content. Pulp protects against the oxidative damage and plays an important role in spermatogenesis. It antihistamine effect can minimize the formation of carcinogenic substance is used for the treatment of prostate cancer (Dhanapal *et al.*, 2012).

(f) Neuroprotective Effect

Neurobehavioral parameters like motor performance (neurological status, significant increase in grasping ability, forelimb strength improvement in balance and co-ordination) are improved after the supplementation of kaitha extract. The biochemical parameters in the brains showed a significant reduction in the total nitrite and lipid peroxidation, also a significant enhanced activity of enzymatic antioxidant such as catalase (Rakhunde *et al.*, 2014).

(g) Wound Healing Activity

Methanol extract of kaitha possess significant dose dependant wound healing and antioxidant activity. It increased wound breaking strength, decreased epithelisation period, increased wound contraction, increased granulation tissue weight and hydroxyproline contraction were observed also increased activity of antioxidant enzymes such as SOD and catalase level were seen. Wound healing activity was statistically significant in animal treatment with extract of kaitha (Iiango and Chitra, 2010).

(h) Other Activities

Pulp extract of kaitha has potent antiulcer activity with lower toxicity. Its antiulcer property probably acts via a reduction in gastric acid secretion (Mishra *et al.*, 2009). Antibiofilm activity of kaitha is also reported. Antibiofilm activity of fruit extract signifying the scope for development of complementary medicine to treat *Aeromonas* biofilm associated infection (Patel *et al.*, 2016).

Conclusion

It is quite evident from this review that kaitha is an important medicinal plant. It contains a number of phytochemicals, which are the key factors contributing medicinal value to this plant. All the major parts of kaitha such as leaf, fruit, seed, bark and root possess wide variety of biological activity and are used to cure a variety of diseases. We have summarized some important pharmacological studies on kaitha with respect to the phytochemical investigations and isolated bioactives from them. Thorough screening of literature available on kaitha depicted the fact that it is a popular remedy for cure of variety of ailments. Further systemic researches are needed to verify their efficacy and their use for the development of food products for their better economic and therapeutic utilization.



Fig.1: Kaitha Fruit

Table 1 Nutritional value of kaitha

Nutrients / sources	Joshi & Jain (2008)	Gopalan et al. (1994)	Morton, (1987)	Jyotsana et al. (2015)	Priyadarshini et al. (2013)	Sharma et al. (2014)	Pandey et al. (2014)	Priyankand Shashi (2008)	Singh et al. (2000)	Kumar et al. (2017)
Moisture (%)	70.6	72.4	74.0	72.4	85.0	76.33	60.4	-	-	-
Protein (%)	7.5	7.1	8.0	7.2	3.19	2.00	13.8	-	-	-
Fat (%)	3.3	0.3	1.45	2.07	-	3.78	4.38	-	-	-
Carbohydrate (%)	22.1	17.0	7.45	15.13	42.2	-	70.4	-	-	-
Fiber (%)	-	-	-	-	11.52crude	-	1.7dietry	-	-	-
Ash (%)	4.6	-	5.0	3.2	8.5	1.32	5.28	-	-	-
Vitamin C (mg/100g)	15.9	3.0	-	66.4	-	-	180	-	-	-
Ascorbic acid (mg/100g)	-	-	-	-	-	7.10	-	-	-	-
Calcium (mg/100g)	-	4.0	-	88.8	-	-	71.18	12.0	-	-
Phosphorus (mg/100g)	-	9.0	-	98.8	-	-	113.73	-	-	-
TSS content (Brix)	-	-	-	13.2	-	11.56	-	-	14.32	20.60
PH	-	-	-	3.4	-	3.50	-	-	4.15	-
Acidity	-	2.3	-	3.18	-	2.92	-	-	-	4.10
Total sugar%	-	-	-	-	-	1.60	-	-	-	-
Reducing sugar %	-	-	-	-	-	1.10	-	-	-	-
Pectin content%	-	-	-	-	-	2.05	-	-	-	-

Table 2: Phytochemical compounds in different parts of Kaitha

	Different Extract	Phytochemical Screening of Kaitha	Sources
L E A V E S	Aqueous extract	Phenols and Glycosides, Saponin, Protein & amino acid, Tannin	Jain et al., 2011
	Ethanol extract	Alcohol, Phenol, Nitrogen compound, Alkaloid, Steroid, Amino acid compound, Tannin, Saponins, Carbohydrate, Gucoside.	Ghumare et al., 2013
	Methanol extract	Phenols, Saponins and Tannins	Saraswathi et al., 2014, Momin et al., 2013
	Acetone extract	Phenol, Tannin	Muthulakashmi et al., 2012
	Ether extract	Terpenoids	Momin et al., 2013
	Chloroform extract	Phytosetol, Phenols, Terpenoids, Phenol, Tannin, Flavonoid	Kapadia et al., 2011
	Petroleum ether	Alkaloid, Glycosides, Phytosterol, Phenol, Tannin, Flavonoid	Jain et al., 2011
B A R K O O T	Methanol extract	Phenol, Nitrogen compound, Vitamin compound, Marmesin Flavanone, Alkaloid, Coumarin, Lignin, Sterol and Triterpene	Attrade et al., 2011 Muthulakashmi et al., 2012, Saraswathi et al., 2014
	Hexane extract	Psoralen, Bergapten, Orientin, Vitexin and Saponarin Osthol, Geranyl, Umbelliferone, Marmin, Marmesin, Aurapten, Bergapten, Isopimpinellin and Peronoil	Attrade et al., 2011

Table 3: Physicochemical analysis of different parts of Kaitha

	Total ash (%)	Water soluble ash (%)	Acid insoluble ash (%)	Water soluble extractive value	Alcohol soluble extractive value	Sources
L E A V E S	9.33	1.83	1.161	-	-	Pandavadra and chanda, 2014
	10.16	0.46	4.13	9.06	5.43	Jain <i>et al.</i> , 2011
	7.30	4.05	2.10	-	-	Ghumare <i>et al.</i> , 2013
S T E M	3.16	0.66	0.66	-	-	Pandavadra and Chanda, 2014

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