



INDO AMERICAN JOURNAL OF PHARMACEUTICAL RESEARCH



PHARMACOLOGICAL PROPERTIES OF *FERONIA LIMONIA* FRUIT PULP – A REVIEW

Win Min Oo, Myat Mon Khine

Department of Biochemistry, University of Medicine-Magway, Myanmar.

ARTICLE INFO

Article history

Received 10/04/2017

Available online
30/04/2017

Keywords

Medicinal Plant,
Feronia Limonia,
Antioxidant,
Anticancer,
Anti-Inflammatory,
Antidiabetic.

ABSTRACT

Current research on drug development has emphasized on traditional uses of herbal constituents which were practiced in ancient times. Many parts of *Feronia limonia* were prescribed for diseases in ancient medicine of Asia. Recently, the active constituents of the fruit pulp have been studied extensively to support the traditional uses. The most important pharmacological actions of the fruit pulp are antioxidant and anticancer activities. These effect may be attributed to its high phenol contents. In-vivo and in-vitro studies of pharmacological effects of the fruit pulp have provided scientific knowledge on its potential use in many diseases such as liver failure, myocardial infarct, ischemic stroke, renal failure, diabetic mellitus and gastric ulcers. This review focuses on pharmacological and medicinal properties of *Feronia limonia* fruit pulp in prevention and treatment of various diseases. The information was gathered from articles which have been published in international journals and which are available online. The outcome of this review provides concise knowledge on pharmacological effects and possible mechanisms which are essential for developing therapeutic uses of the fruit pulp. It can be concluded that *Feronia limonia* fruit pulp has various pharmacological actions which can be utilized in treatment of many diseases if the active constituents for respective actions are identified in the future.

Corresponding author

Win Min Oo

No (91), 19th street, Yanpel Quarter,
Magway, Myanmar. 90101,
drwinminoo.umm@gmail.com
+9595340338

Please cite this article in press as **Win Min Oo et al.** Pharmacological Properties of *Feronia Limonia* Fruit Pulp – A Review. *Indo American Journal of Pharmaceutical Research*.2017;7(04).

INTRODUCTION

Feronia limonia (*Limonia acidissima* Linn, *Schinus limonia* Linn, or *Feronia elephantum*) is a moderate-sized tree which belongs to the family Rutaceae. It is widely distributed in Asia particularly India, Sri Lanka and Myanmar. It has different names in different regions such as Kaitha in Hindi, Thakaka in Myanmar, wood apple in English and Kavita in Bangladesh. Many parts of the tree such as leaves, barks, fruits, roots and gums have been prescribed in traditional medicine for many ailments [1]. In recent years, researchers took interest in the pharmacological roles of fruit pulp of *Feronia limonia*.

Phytochemical and spectroscopic analysis of ripe fruit of *Feronia limonia* has stated the presence of carbohydrates, steroids, flavonoids, tannins, glycosides, saponins, alkaloids, phenols, acidic compounds [2-4]. According to chemical analysis, 2.43% protein, 42.2% carbohydrate, 29% lipid, 85% moisture, 11.52% fiber and 8.5% ash are present in the fruit pulp [5]. The fruit pulp contains higher amounts of proteins and carbohydrates as compared with other parts of the tree [6]. Tyramine derivatives, coumarins, luteolin and flavone glycoside have been identified and isolated from the fruit of *Feronia limonia* [7-11].

The potential use of the fruit pulp in medicine is challenging. *In vivo* and *in vitro* studies have supported the ancient use of *Feronia limonia* in various diseases. However, the medicinal properties of the fruit pulp has not been reviewed systematically in literature. This purpose of this article is to review the pharmacological and medicinal properties of *Feronia limonia* fruit pulp, which have been reported in recent researches. This review supports the traditional use in Ayurveda medicine and contribute systematic information on therapeutic potential for the diseases.

Antioxidant properties

Feronia limonia fruit extracts become interested for antioxidant properties. Dietary intake of 3% dry powder for one to two months increased the activities of antioxidant enzymes such as superoxide dismutase (SOD), glutathione peroxidase (GPx) and glutathione S-transferase (GST) and reduced lipid peroxidation in serum, hepatic and muscle tissues of *Cyprinus carpio* fish models. The effect on SOD activity was more marked in the liver while activation in GPx and GST by the extract was prominent in the muscle [12].

Although different types of extracts (methanol, water, ethyl acetate and chloroform-based) have been stated to have antioxidant activities, methanol extract is the most effective against DPPH (2,2-Diphenyl 1-Picrylhydrazyl) radicals and hydroxyl radicals. Methanol extract has the highest TEAC (Trolox Equivalent Antioxidant Capacity) value, FRAP (Ferric Reducing Antioxidant Power), TAA (Total Antioxidant Activity) as compared with other kinds of extracts. On another hand, water extract of the fruit is the most powerful scavenger against nitric oxide compared with other extracts [5]. Hydroxyl radical scavenging and metal chelating effects of the fruit pulp were inferior to those of rind and leaf extract respectively [13].

Antioxidant action of *Feronia limonia* fruit alleviates oxidative stress in different organs. Carbon tetrachloride (CCl_4) induced oxidative stress in testicular tissues of rats was indicated by decline in CAT, SOD, GSR, GST and GSH, and increased H_2O_2 and TBARS in tissue homogenates. Treatment with 100mg/kg and 400mg/kg of methanolic extract for 7 days significantly attenuated oxidative markers and enhanced antioxidant enzyme activities [14]. Similarly, CCl_4 induced oxidative stress in hepatic tissues was tempered by oral intake methanolic extract of the fruit [15]. *Feronia limonia* also raised glutathione level and lessened oxidative stress in paracetamol poisoning [16]. In the study of Ilango and Chitra (2009), the extract was found to reverse the oxidative stress in pancreatic homogenate of alloxan-induced diabetic rats [17].

Antioxidant property of *Feronia limonia* fruit pulp is mainly due to its high phenol content although it also contains ascorbic acid in lesser amount [18]. Methanol extract of fruit pulp contains 76.77 to 351.45 mg GAE/g at concentrations ranging from 1.25 to 10 mg/ml. Total phenol content has strong positive correlations with DPPH scavenging ($r=0.98$), ABTS ($r=0.99$) and TAA ($r=0.98$) [19].

Anticancer properties

Methanolic extract of *Feronia limonia* was shown to have anticancer effects. It promoted percent cell death, percentage increase in life span and prolonged mean survival time in mice with Dalton's ascitic lymphoma. *Feronia limonia* methanolic extract not only reduced tumor cell growth but it also decreased solid tumor volume and percentage increase in solid tumor (%IST). These may be attributed to cytotoxic and anti-proliferative properties of *Feronia limonia*. Interestingly, restoration of hematological parameters (rise in hemoglobin and red cell count, and fall in WBC count) indicated that *Feronia limonia* extract is not associated with myelosuppression, which is a major problem encountered in some chemotherapy [2].

Luteolin isolated from the fruit pulp was proved to possess apoptosis-inducing and cytotoxic effects. Treatment with 50 $\mu\text{g/ml}$ and 100 $\mu\text{g/ml}$ of the extract reduced number of cell viability and induced apoptosis in human hepatocellular carcinoma (HepG2) cell lines. Cytotoxic action of luteolin was comparable with that of vincristine. The maximal anti-cancer effect was observed as IC_{50} 48.23 % inhibition at 100 $\mu\text{g/ml}$ of the extract [20].

The cytotoxic action of *Feronia limonia* on human lung cancer H460 cell line was observed by Tripathy and colleagues in 2016. Methanolic extract had an IC_{50} of 46.21%. With the extract concentration ranging from 40 to 160 $\mu\text{g/ml}$, there was no evidence of hemolysis, which is one of limiting factors to use natural products as chemotherapy [21].

Anti-mutagenic actions were observed mainly in phenolic glycosides followed by ester-bound and free phenolics of *Feronia limonia*. Anticyanidins which is released in acid hydrolysis of fruit pulp are responsible for anti-mutagenic action. In addition, anti-mutagenic effect of *Feronia limonia* extract is strongly correlated with total phenol contents [3].

Ethanollic extract of *Feronia limonia* arrests the cell cycle of tumor cells. 160µg/ml of the extract was able to block S phase by reducing S phase population from 12.89 to 7.19% in breast cancer cell line SKBR3. Cell cycle of breast cancer MDA-MB-435 was susceptible to G2/M blockage from 24.41 to 45.65% by a concentration of 120µg/ml of ethanollic extract compared with control [22-23].

Cytotoxic action of *Feronia limonia* exhibits a dose-dependent manner [24]. *In-vitro* treatment of breast cancer cell line MCF-7 with different concentrations of methanolic extracts of *Feronia limonia* significantly suppressed cancer cell growth in a dose-dependent way with the maximal inhibition of 79.69% at 1,000µg/ml of the extract [25].

Previous *in-vivo* and *in-vitro* studies indicated that *Feronia limonia* is a potential chemotherapeutic agent against breast cancers, lung cancers and lymphomas, and supported the ancient of the fruit in the treatment of cancers. However, additional purification of specific compounds of the fruit pulp is needed to widen its use against cancers.

Antidiabetic and antihyperlipidemic properties

Studies have reported *Feronia limonia* has a significant hypoglycemic effect *in-vivo*. A single dose of *Feronia limonia* extract lowered blood glucose level in normal fasted state and normal fed state, and in diabetic condition [26-27]. Histological analysis of the pancreas after a single administration of the extract suggested that the extract lowered blood glucose level by induction of insulin secretion because the degranulation in beta cells were observed [26].

Daily intake of the extract of *Feronia limonia* fruit pulp improved glycemic status significantly in animal models with diabetic mellitus in 3 to 4 weeks. The results were comparable with those of metformin and sulfonylurea. As antidiabetic effect of *Feronia limonia* extract was inferior to standard treatment (Metformin and sulfonylurea), isolation of the moiety which is the most responsible for antidiabetic action is still required for potential therapeutic use [17, 27-30].

Antidiabetic effect of the extract could be explained by increased insulin secretory granule synthesis and increased secretion of insulin, restoration of pancreatic antioxidant enzyme activities (superoxide dismutase, catalase), reduction of oxidative stress (MDA), decline in activity of glucose 6-phosphatase and stimulation of hepatic hexokinase activity and increased glycogen content [17,31].

Diabetic mellitus is usually associated with abnormal lipid profile. *Feronia limonia* fruit extract lowers total cholesterol, triacylglycerol, LDL and VLDL levels, and raises HDL level in diabetic mellitus [29,31]. The antihyperlipidemic effects can be explained with different mechanisms. Saponins and phytosterols can inhibit pancreatic lipase and reduce intestinal absorption of lipids. Fibers of the extract can lower LDL level. In addition, flavonoids and ascorbate increases HDL and decrease LDL [31].

Anti-inflammatory, analgesic and antipyretic properties

Methanolic extract of *Feronia limonia* fruit has anti-inflammatory, analgesic and antipyretic activities. Ahamed and colleagues (2008) reported that the extract significantly inhibited carrageenan-induced paw edema and cotton pellet granuloma formation in animal models. It was shown to be dose-dependent and comparable with the effects of ibuprofen. It may be suggested that the mechanism of inhibition is likely at the level of lipooxygenase enzyme without affecting cyclooxygenase enzyme as the extract failed to suppress arachidonic acid induced paw edema like indomethacin. The extract was able to reduce acetic acid induced writhing and unable to exert analgesic effect on hot plate induced pain in mice. Thus, the analgesic property of *Feronia limonia* is the same as non-narcotic analgesics. In addition, the extract had a significant reduction of pyrexia in animals induced with Brewer's yeast [32].

Immunomodulatory properties

Methanolic extract of the fruit also has immunomodulatory functions. It can enhance phagocytic action of macrophages, activate lysosomal enzymes and accelerate proliferation of splenocytes [33].

Wound healing properties

Topical and oral administration of *Feronia limonia* fruit extract accelerates wound healing. According to experimental study, the possible mechanisms are increased wound contraction, rise in hydroxyproline content, accelerated granulation tissue formation, increased fibroblasts and fibrosis, and increased activities of antioxidant enzymes [34].

Hepatoprotective properties

Feronia limonia has been used as liver diseases in Asia for centuries. Many studies have reported that the extract of fruit pulp has both hepatoprotective and curative activities against hepatotoxicities [16].

In paracetamol overdose, accumulation of NAPQI (N-Acetyl P-Benzoquinimine) induces oxidative stress and subsequent membrane damage, and hepatocyte necrosis. Treatment with *Feronia limonia* extract (300-400 mg/kg for 10 days) after toxicity increased hepatic antioxidant enzyme activities and restoration of raised liver enzymes in experimental animals with paracetamol toxicity. Histological features of the liver were consistent with regeneration and recovery of damaged liver parenchyma [16,35]. It may be due to replenishment of reduced glutathione (GSH) which is essential to metabolize NAPQI as dietary intake of *Feronia limonia* fruit powder can raise hepatic GSH level [36].

Similarly, *Feronia limonia* extract protects against damaging effects of carbon tetrachloride (CCl₄). Underlying mechanisms seem to be activation of antioxidant enzymes (SOD, catalase etc.), membrane stabilization and regeneration of hepatocytes according to biochemical and histological results [34,37-38]. Ferolactone (furanocoumarin described as monoterpenoid-5-methoxy furanocoumarin lactone) from the fruit pulp has been reported to have a significant anti-hepatotoxic effect against CCl₄ induced liver damage [39]. *Feronia limonia* fruit powder also protects fluoride-induced oxidative damage in mice [36].

Neuroprotective properties

Methanolic extract of *Feronia limonia* may be a potential therapeutic for ischemic induced brain injury. Rakhunde and coworkers determined neuroprotective effects of methanolic extract on ischemia reperfusion induced brain injury in mice. Neurological behaviors such as motor performance were significantly improved by administration of 500mg/kg BW of ethanolic extract. In addition, total nitrite and lipid peroxidation were suppressed and antioxidant enzyme activities such as SOD and catalase were activated by the intake of *Feronia limonia* extract [40].

Nephroprotective and diuretic properties

Vasant and Narasimhacharya (2011) investigated the effect of *Feronia limonia* fruit powder on fluoride-induced oxidative stress in rats. Sodium fluoride led to increased oxidative stress in renal tissues as there were a rise in TBAR and a fall in TAA, SOD, CAT, GSH and GPx activities. *Feronia limonia* fruit powder showed a dose-dependent improvement in antioxidant activities and reduction of lipid peroxidation in renal tissue homogenate. 10g% dose was found to be more effective than 2.5 g% and 5g% extract powder [36].

Animal studies demonstrated that 200 to 400 mg/kg p.o. for 21 days reduced serum creatinine and blood urea nitrogen (BUN) in alloxan-induced diabetic rats. It also raised serum total protein level suggesting that it might suppress proteinuria in diabetic state [17].

Methanolic extracts of *Feronia limonia* fruit obtained via the Microwave-assisted extraction (MAE) and Bath Sonicator extraction (BSE) had diuretic effect on experimental mice. Single dose of 50%w/w p.o. significantly increased urine output 5 hours after administration. Urinary excretions of sodium, potassium and chloride ions were also enhanced. The diuretic action of *Feronia limonia* fruit was comparable with that of furosemide and supports the traditional use of the fruit as a diuretic [41].

Cardioprotective properties

Manohar and coworkers (2016) determined cardioprotective effects of *Feronia limonia* on Isoproterenol-induced myocardial infarct in rats. 200 to 400 mg/kg BW of ethanolic extract of *Feronia limonia* fruit pulp significantly reduced creatinine phosphokinase (CK) and lactate dehydrogenase (LDH) in the blood, while it activated SOD and CAT activities in myocardial homogenate [42]. These findings suggest cardioprotective property of the fruit pulp in myocardial infarct, which may be attributable to antioxidant properties of phenols in *Feronia limonia* fruit.

Anti-asthmatic properties

Feronia limonia has been reported to have anti-asthmatic action. Treatment with ethanolic extract relaxed tracheal chains of guinea pigs *in-vitro* study. It exhibited a concentration dependent manner. However, 1 g/100 ml of ethanolic extract had relaxant action which was significantly inferior to that of theophylline [43]. Proper identification of the compounds in the extract which have anti-asthmatic action are under investigations.

Antibacterial properties

Methanol extract of *Feronia limonia* has antibacterial action on various clinical pathogens. In the study of Hossain (2013), *Salmonella paratyphi* B and *Salmonella paratyphi* showed maximal zone of inhibition as compare with other organisms. However, the effect was inferior to that produced by Kanamycin used as a standard [24].

Ponnuraj and coworkers (2015) reported on the dose-dependent inhibition of methanol extract on Gram positive and Gram negative bacteria and 500mg/ml was the concentration responsible for maximal inhibitions. Surprisingly, the efficacies against *Salmonella typhi* and *Vibrio cholera* were the same at 100 to 500mg/ml. there was no inhibitory effect on *Bacillus cerius* at lower concentrations [4].

Among Gram positive bacteria, *Staphylococcus aureus* was more susceptible to the extract while *Klebsiella pneumoniae* was more sensitive than other Gram negative microorganisms [44].

Among the different parts of *Feronia limonia* tree, fruit pulp extract was shown to have greater antibacterial action than other parts such as bark, leaves, roots etc. [6].

Antibacterial action of the fruit has created the hope that it can be used as an alternative in treatment of antibiotic resistant bacteria. However, as there as many phytochemicals in the fruit extract, identification and isolation of proper antibacterial component is still needed.

Antiulcer properties

Mishra and colleagues (2009) investigated the effect of *Feronia limonia* extract on indomethacin-induced ulcers in albino rats. Pretreatment with 500mg/kg ethanolic extract reduced gastric ulcer risks in rats after intraperitoneal administration of indomethacin. Though the effect of the extract was lower than that of ranitidine, it was proved to have antiulcer activity by means of suppression of gastric acid secretion and raising gastric pH. Their study supported the indigenous use of *Feronia limonia* to treat peptic ulcer in folk medicine [45].

Antispermatogetic and antisteroidogenic properties

Feronia limonia fruit extract has been described as antispermatogetic and antisteroidogenic in animal models. It decreased epididymal sperm count, motility, viability, epididymal and testicular protein content. It reduced the activities of glucose 6-phosphate dehydrogenase and Δ^5 -3 β -hydroxy steroid dehydrogenase. However, reversibility was confirmed 5 days after treatment withdrawal. These findings support the indigenous utilization of *Feronia limonia* fruit pulp as male contraceptive [46].

CONCLUSION

The pharmacological properties of *Feronia limonia* fruit pulp have been studied extensively in recent years. The findings of these studies support the traditional use of the fruit pulp in various ailments. However, the active ingredients which exert respective pharmacological actions need to be identified and isolated so that the fruit pulp may be used in medical treatment in the future. It is recommended that other parts of *Feronia limonia* such as leaves and bark should be reviewed for their potential therapeutic uses.

Conflict of interest

The authors declare that there is no conflict of interest in the subject matter or materials described in this manuscript.

Source of funding

The authors declare that there is no source of funding to write this review.

Abbreviations

ABTS	:2, 2'-Azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) diammonium salt
BSE	:Bath Sonicator extraction
BUN	:Blood urea nitrogen
BW	:Body weight
CAT	:catalase
CCl ₄	:Carbon tetrachloride
CK	:Creatinine phosphokinase
DPPH	:2,2-Diphenyl 1-Piclyhydrazyl radicals
FRAP	:Ferric Reducing Antioxidant Power
g	:Gram
GAE	:Garlic acid equivalent
GPx	:Glutathione peroxidase
GSH	:Reduced glutathione
GSR	:Glutathione reductase
GST	:Glutathione S-transferase
H ₂ O ₂	:Hydrogen peroxide
HDL	:High density lipoprotein
IC ₅₀	:Half maximal inhibitory concentration
IST	:Increase in solid tumor
kg	:Kilogram
LDH	:Lactate dehydrogenase
LDL	:Low density lipoprotein
MAE	:Microwave-assisted extraction
MDA	:Malondialdehyde
μg	:Microgram
mg	:Milligram
ml	:Milliliter
NAPQI	:N-Acetyl Para-benzoquinimine
p.o.	:Per oral
SOD	:Superoxide dismutase
TAA	:Total Antioxidant Activity
TBARS	:Thiobarbituric acid reactive substances
TEAC	:Trolox Equivalent Antioxidant Capacity
VLDL	:Very low density lipoprotein
w/w	:Weight by weight, WBC :White blood cell

REFERENCES

1. Qureshi AA, Kumar K, Eswar, Shaista O. *Feronia limonia* - a path less travelled. *International Journal of Research in Ayurveda & Pharmacy* 2010;1(1):98-106.
2. Eluru JR, Taranalli AD, Kawatra S. Anti-tumor activity of *Limonia acidissima* L. methanolic extract in mice model of Dalton's ascitic lymphoma. *International Journal of Pharmacognosy and Phytochemical Research* 2015;7(6):1094-1100.
3. Phapale R, Thakur SM. Antioxidant activity and antimutagenic effect of phenolic compounds in *Feronia limonia* (L) in swingle fruit. *International Journal of Pharmacy and Pharmaceutical Sciences* 2010;2(4):68-73.
4. Ponnuraj S, Jaganathan D, Kanagarajan M, Deivamarudachalam, TPD. Spectroscopic analysis and antibacterial efficacy of bioactive compounds from *Limonia acidissima* L. fruit extract against clinical pathogens. *International Journal of Pharmacy and Pharmaceutical Sciences* 2015;7(3):383-389.
5. Darsini DTP, Maheshu V, Vishnupriya M, Nishaa S, Sasikumar JM. Antioxidant potential and amino acid analysis of underutilized tropical fruit *Limonia acidissima* L. *Free Radicals and Antioxidants* 2013;3:562569.
6. Thomas A, Ponnammal NR. Preliminary studies on phytochemical and antibacterial activity of *Limonia acidissima* (L) plant parts. *Ancient Science of Life* 2005;25(2):57-61.
7. Ghosh P, Sil P, Majumda SG, Thakur S. A coumarin from *Limonia acidissima*. *Phytochemistry* 1982;21:240-241.
8. Chatterjee A, Sankar S, Shoolery JN. 7-phenyl acetoxycoumarin from *Limonia crenulata*. *Phytochemistry* 1980;19:2219-2220.
9. Parthasarathi G, Prabal S, Swapnadip T, Kokke WCMC, Akihisa T, Shimizu N et al. 1991. Tyramine derivatives from the fruit of *Limonia acidissima*. *J. Nat. Prod.* 1991;54:1389-1393.
10. Hanchinalmath JV, Londonkar R. Cytotoxic and apoptosis-inducing effect of luteolin isolated from *Feronia limonia* on HepG2 cells. *Biolife journal* 2014;2(4):1287-1292.
11. Dar AI, Masar G, Jadhav V, Bansal K, Saxena RC. Isolation and structural elucidation of the novel flavone glycoside from *Feronia limonia* L. *Journal of pharmacy research* 2013;30:1-8.
12. Darsini DTP, Srinivasan V, Maheshu P, Nishaa S, Castro J. Dietary supplementation of *Limonia acidissima* L. fruit on in vivo. Singapore: IACST Press. 2013;57:73-79. doi:10.7763/IPCBE.2013.V57.14.
13. Nachimuthu S, Kumaravel V, Sadhasivam S, Santhosharajan N, Peraman M, Ponnusamy R. Phytochemical screening and evaluation of antioxidant potential of *Feronia limonia* leaves and fruit extracts. *Journal of Chemical and Pharmaceutical Sciences* 2014;2(2):36-40.
14. Hanchinalmath JV, Londonkar R. In-vitro antioxidant activity of *Feronia limonia* in rat testicular homogenate. *Int. J. Pharm. Sci. Rev. Res.* 2014;27(1):168-171.
15. Ilango K, Chitra V. Hepatoprotective and antioxidant activities of fruit pulp of *Limonia acidissima* Linn. *International Journal of Health Research* 2009;2(4):361-367.
16. Qureshi AA, Kumar E. Evaluation of antioxidant and hepatoprotective potential of *Feronia limonia* in rats. *European journal of pharmaceutical and medical research* 2016;3(7):471-479.
17. Ilango K, Chitra V. Antidiabetic and antioxidant activity of *Limonia acidissima* Linn. in alloxan induced rats. *Der Pharmacia Lettre* 2009;1(1):117-125.
18. Sonawane S, Arya SS. Antioxidant activity of Jambhul, Wood Apple, Ambadi and Ambat Chukka: an indigenous lesser known fruits and vegetables of India. *Advance Journal of Food Science and Technology* 2013; 5 (3): 270-275.
19. Hanchinalmath JV, Londonkar R. In-vitro antioxidant activities of *Feronia limonia* Linn. *Indo American Journal of Pharmaceutical Research* 2014; 4 (6): 2937-2942.
20. Hanchinalmath JV, Londonkar R. Cytotoxic and apoptosis-inducing effect of luteolin isolated from *Feronia Limonia* on HepG2 cells. *Biolife journal* 2014; 2 (4), 1287-1292.
21. Tripathy G, Pradhan D, Pradhan S, Dasmohapatra T. Evaluation of plant extracts against lung cancer using H460 cell line. *Asian journal of pharmaceutical and clinical research* 2016; 9 (2): 227-229.
22. Pradhan D, Tripathy G, Patnaik S. Screening of antiproliferative effect of *Limonia acidissima* Linn. fruit extracts on human breast cancer cell lines. *African Journal of Pharmacy and Pharmacology* 2012; 6 (7): 468-473.
23. Pradhan D, Tripathy G, Patanaik S. Anticancer activity of *Limonia acidissima* Linn (Rutaceae) fruit extracts on human breast cancer cell lines. *Tropical Journal of Pharmaceutical Research* 2012; 11 (3): 413-419.
24. Hossain MS. Evaluation of antimicrobial and cytotoxic activity of the plant extracts of *Feronia limonia* (Linn). *Journal of Scientific and Innovative Research* 2013; 2 (5): 859-863.
25. Tripathy G, Pradhan D. In vitro anti breast cancer activity of *Limonia acidissima* against MCF-7 cell line. *World Journal of Pharmacy and Pharmaceutical Sciences* 2015; 4 (4): 1543-1550.
26. Gupta R, Johri S, Saxena AM. Effect of ethanolic extract of *Feronia elephantum* Correa fruits on blood glucose levels in normal and streptozotocin induced diabetic rats. *Normal Product Radiance* 2009; 8 (1): 3236.
27. Mishra A, Garg GP. Antidiabetic activity of fruit pulp of *Feronia elephantum* Corr. *Pharmacognosy Journal* 2011; 3 (20): 27-32.
28. Kangralkar VA, Patil-Shivraj D, Khatib N. Hypoglycemia effect of aqueous extract of *Feronia elephantum* fruits. *International Journal of Pharmaceutical Sciences Review and Research* 2010; 4 (1): 64-66.
29. Priya EM, Gothanda AM, Karthikeyan S. Antidiabetic Activity of *Feronia limonia* and *Artocarpus heterophyllus* in Streptozotocin induced diabetic rats. *American Journal of Food Technology* 2012; 7 (1): 43-49.
30. Narasimhacharya, Rupal A Vasant, Amaravadi VRL. *Limonia* fruit as a food supplement to regulate fluoride-induced hyperglycaemia and hyperlipidaemia. *J Sci Food Agric* 2013, 93: 422-426.

31. Vasant RA, Narasimhacharya AVRL. Limonia fruit as a food supplement to regulate fluoride-induced hyperglycaemia and hyperlipidaemia. *J Sci Food Agric* 2013; 93 :422-426
32. Ahamed SM, Swamy SK, Jayaverra KN, Rao VJ, Kumer VS. Antiinflammatory, antipyretic and analgesic activity of methanolic extreact of *Feronia limonia* fruit pulp. *Pharmacologyonline* 2008; 3: 852-857.
33. Tripathy G, Pradhan D. Estimation of immunomodulatory activity of *Feronia limonia* Linn. *Asian journal of pharmaceutical and clinical resesarch* 2014; 7 (1): 219-221.
34. Ilango K, Chitra V. Wound healing and anti-oxidant activities of the fruit pulp of *Limonia acidissima* linn (rutaceae) in rats. *Tropical Journal of Pharmaceutical Research* 2010; 9 (3): 223-230.
35. Dar AI, Saxena RC, Bansal SK. Assessment of hepatoprotective activity of fruit pulp of *Feronia limonia* (Linn.) against paracetamol induced hepatotoxicity in albino rats. *J. Nat. Prod. Plant Resour* 2012; 2 (2): 226-233.
36. Vasant RA, Narasimhacharyaa AVRL. Alleviaiton of fluoride-induced hepatic and renal oxidative stress by the fruit of *Limonia acidissima*. *Fluoride* 2011; 44 (1): 14-20.
37. Hanchinalmath JV, Londonkar R. Anti hepatotoxicity studies of crude extract of *Feronia limonia* in CCl₄ induced toxicity. *World journal of pharmacy and pharmaceutical sciences* 2014; 3 (7): 1536-1546.
38. Upadhyay R, Pandey ND, Narvi SS, Verma A, Ahmed B. Antihepatotoxic effect of *Feronia limonia* fruit against carbon tetrachloride induced hepatic damage in albino rats. *Chinese Medicine* 2010; 1: 19-22.
39. Upadhyay R, Verma A, Pandey ND, Narvi SS. Antihepatotoxic activity of ferolactone, a new furanocoumarin from *Feronia limonia*. *Med Chem Res* 2012; 21: 2955-2960.
40. Rakhunde PB, Saher S, Ali SA. Neuroprotective effect of *Feronia limonia* on ischemia reperfusion induced brain injury in rats. *Indian journal of pharmacology* 2014; 46 (6): 617-621.
41. Parial S, Jain DC, Joshi S. Diuretic activity of the extracts of *Limonia acidissima* in rats. *Rasyan J. Chem.* 2009. 2 (1) : 53-56.
42. Manohar HD, Srinivansan D, Sengottuvelu S. Cardoprotective activity of *Limonia acidissima* against isoproterenol induced myocardial infarction in rats. *Research journal of pharmacy and technology* 2016;9 (5) : 541-544.
43. Mahapatra PK, Pradhan D. Relaxant effects of *Limonia acidissima* Linn (pulp) on guinea pig tracheal chains and its possible mechanisms. *Int J Pharm Pharm Sci* 2014; 6 (5): 257-263.
44. Nithya N, Saraswathi U. In vitro antioxidant and antibacterial efficacy of *Feronia elephantum* Correa fruit. *Indian journal of natural products and resources* 2010; 1 (3): 301-305.
45. Mishra A, Arora S, Gupta R, Manvi R, Punia J, Sharma AK. Effect of *Feronia elephantum* (Corr) fruit pulp extract on indomethacin-induced gastric ulcer in albino rats. *Tropical journal of pharmaceutical research* 2009; 8 (6): 509-514.
46. Dhanapal R, Ratna JV, Sarathchandran I, Gupta M. Reversible antispermatogetic and antisteroidogenic activities of *Feronia limonia* fruit pulp in adult male rats. *Asian Pacific Journal of Tropical Biomedicine* 2012; 2 (9): 684-690.



54878478451170421



Submit your next manuscript to **IAJPR** and take advantage of:

Convenient online manuscript submission

Access Online first

Double blind peer review policy

International recognition

No space constraints or color figure charges

Immediate publication on acceptance

Inclusion in **Scopus** and other full-text repositories

Redistributing your research freely

Submit your manuscript at: editorinchief@iajpr.com

