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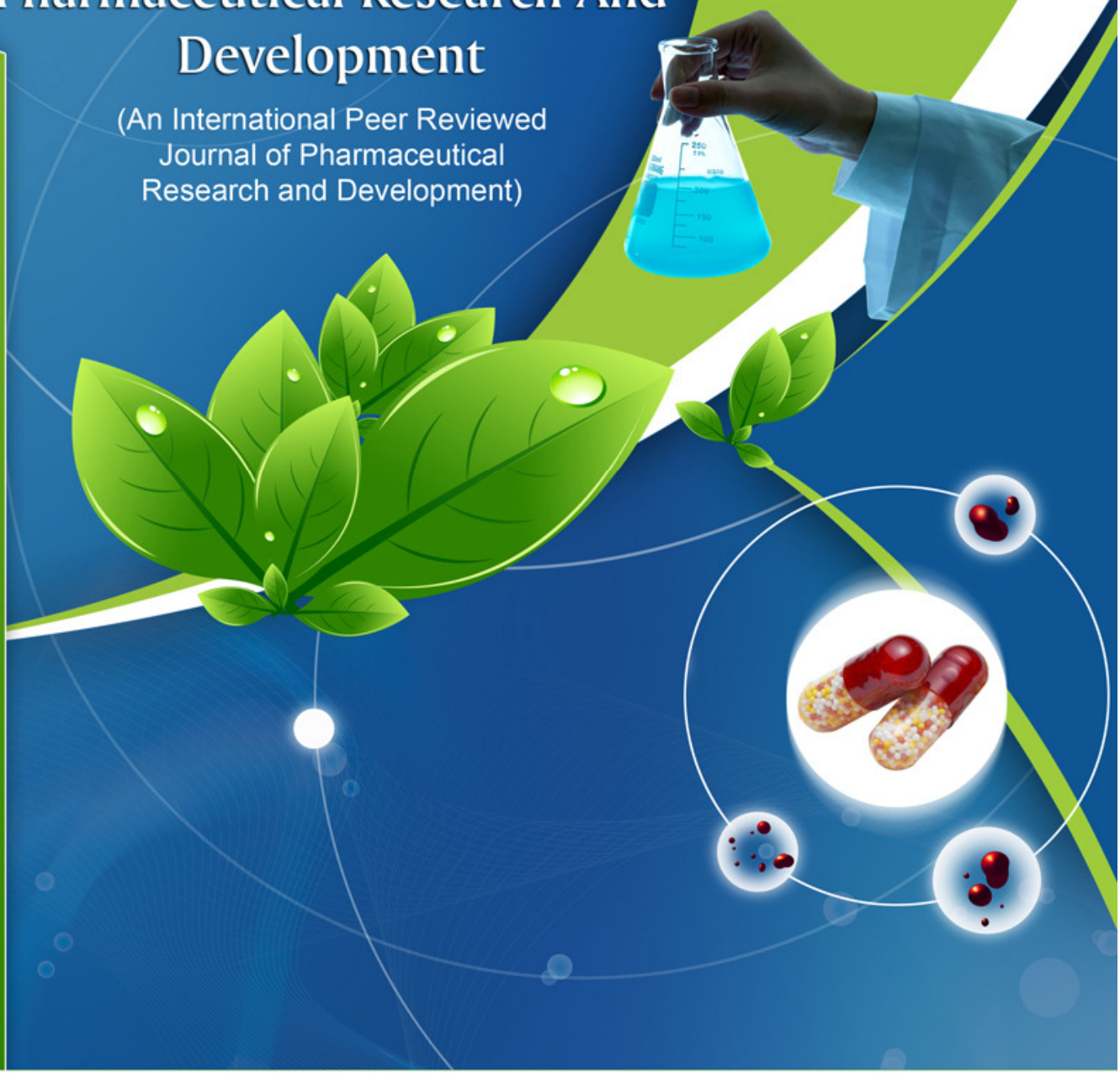

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Review Article

THE NATURE'S POTENTIAL MULTIPURPOSE GIFT – PAPAYA (*CARICA PAPAYA LINN.*): A COMPLETE OVERVIEW

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ABSTRACT

Papaya (Carica papaya Linn.), an herbaceous fruit crop belonging to the family Caricaceae, has garnered popularity among researchers due to its nutritional and potent pharmacological value. It is often seen in orange-red, yellow-green and yellow-orange hues, with a rich orange pulp. The fruit is not just delicious and healthy, but whole plant parts, fruit, roots, bark, peel, seeds and pulp are also known to have medicinal properties. It is regarded as an excellent source of ascorbic acid, a good source of carotene, riboflavin and a fair source of iron, calcium, thiamin, niacin, pantothenic acid, vitamin B-6 and vitamin K. Several studies on different parts of carica papaya material used in extracting were highlighted. Extracts from different parts of Carica papaya plant have shown their positive effects when used as anti-microbial, anti-oxidant, anti-malarial, anti-ulcer, anti-HIV, anti-inflammatory, anti-cancer, anti-hypertensive, anti-fertility, anti-fungal and anti-diabetic. In the present review nutritional value of the Carica papaya and wide pharmacological properties of its various parts in different extracts have been discussed to provide collective information on this multipurpose commercial fruit crop.

***Key words**: Papaya, Carica papaya, Nutritional, Pharmacological Value*

INTRODUCTION

Carica papaya is a member of the Caricaceae and is a dicotyledonous, polygamous, and diploid species [1]. It originated from Southern Mexico, Central America, and the northern part of South America. It is now cultivated in many tropical countries such as Bangladesh, India, Indonesia, Sri Lanka, Philippines, and West Indies [2]. The plant is native to tropical America [3] and was introduced to India in 16th century. The plant is recognized by its weak and usually unbranched soft stem yielding copious white latex and crowded by a terminal cluster of large and long stalked leaves, is rapidly growing and can grow up to 20 m tall [4, 5].

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It may cultivate for its young leaves, shoots and fruits which are cooked as a vegetable or for its ripe fruit which is well known as a popular beverage [6]. Young leaves are rich in flavonoids (kaempferol and myricetin) [7], alkaloids (carpaine, pseudocarpaine, dehydrocarpaine I and II) [8], phenolic compounds (ferulic acid, caffeic acid, chlorogenic acid), the cynogenetic compounds (benzylglucosinolate) found in leaves [9]. The papaya fruit, as well as all other parts of the plant, contain a milky juice in which an active principle known as papain is present. Aside from its value as a remedy in dyspepsia and kindred ailments, it has been utilized for the clarification of beer. The juice has been in use on meat to make it tender [10]. The seed is used for intestinal worms when chewed. The root is chewed and the juice swallowed for cough, bronchitis, and other respiratory

diseases. The unripe fruit is used as a remedy for ulcer and impotence [11].

NUTRITIONAL VALUE

The economic and nutritional potential of the plant has made it a fruit and vegetable of choice. Papaya is a first rate source of vitamins A and C. It contains in small quantity thiamine, riboflavin, calcium, iron, potassium, magnesium and sodium [12]. One beneficial effect of seeds of Carica papaya is its ability to cure intestinal worms when chewed. Carica papaya fruit is used in remedying dyspepsia, utilized for the clarification of beer as well as the usage of the juice in meat tendering [13]. Treatments of sickle cell diseases and poisoning related disorder is a possibility using seeds of Carica papaya [14, 15]. It has been reported that the nutritive value of cooked food is lower in comparison to uncooked food [16]. The leaf tea or extract has a reputation as a tumor destroying agent [17]. The fresh green tea is an antiseptic whilst the brown, dried pawpaw leaves are best as a tonic and blood purifies [18]. The tea also promotes digestive and aid in treatment of ailment such as chronic indigestion, overweight and obesity, arteriosclerosis, high blood and weakening of the heart [19].

Nutritionally, the major components of pawpaw fruit pulp dry matter are carbohydrates. The total dietary fibre content of ripe fruit varies from 11.9 to 21.5 g/ 100g/ dry matter crude protein ranges from 3.74 to 8.26 g/ 100 dry matters [20- 22]. There are two main types of carbohydrates in pawpaw fruits, the cell wall polysaccharides and soluble sugars. At the early stage of fruit development, glucose is the main sugar but the sucrose content increases during ripening and can reach up to 80% of the total sugars [23]. Low vitamin C content was observed in the seed and peel, but the pulp had relatively higher vitamin C (0.11-0.15mg) and vitamin A at different stages of ripening [24].

MEDICINAL AND PHARMACOLOGICAL PROPERTIES

Anti-cancer

Petroleum ether (40-60^0 C), Chloroform, ethyl acetate and methanol 80% extracts of C. papaya aerial parts were tested for their anti cancer activity on three cancer cells TK10 (renal), UACC62 (melanoma) and MCF7 (breast) cancer cells using a Sulforhodamine B (SRB) assay. Petroleum ether of C. papaya at the concentration of 100µg/ml has shown a significant anticancer effect for MCF7 (breast) cancer cells and showed less anticancer effect for the other two cancer cells while the other extracts have mild anticancer effect on the three cancer cells [25].

Various parts of Carica papaya Linn. (CP) have been traditionally used as ethnomedicine for a number of disorders, including cancer. Study was conducted to examine the effect of aqueous-extracted CP leaf fraction on the growth of various tumor cell lines and on the anti-tumor effect of human lymphocytes. Result showed significant growth inhibitory activity of the CP extract on tumor cell lines. In PBMC, the production of IL-2 and IL-4 was reduced following the addition of CP extract, whereas that of IL- 12p40, IL-12p70, IFN-_ and TNF-_ was enhanced without growth inhibition [26].

Anti- inflammatory

The anti-inflammatory activity of an ethanolic extract of Carica papaya leaves was investigated in rats using carrageenan induced paw oedema, cotton pellet granuloma and formaldehyde induced arthritis models. The results showed that the extracts significantly ($p < 0.05$) reduced paw oedema in the carrageenan test [27].

Anti-inflammatory effect of Carica Papaya Aqueous seed extract (3 doses of 5mg/kg, 10mg/kg, 20mg/kg) was assessed comparing their effect with Aspirin in albino rats by inducing acute Inflammation – by Carrageenan-induced rat paw edema method. Carica Papaya Aqueous seed extract treated groups with 10mg/kg and 20mg/kg has showed significant reduction in paw edema volume at 5 hours when compared to control group in acute inflammation method. These findings indicate that Carica Papaya Aqueous seed extract was exhibiting more anti-inflammatory effect in comparison with aspirin (standard) [28].

Anti-microbial

The high antimicrobial activity for the extracts of C.papaya in petroleum ether with a Minimun Inhibitory Concentration was found to be 2mg/ml as against 4mg/ml and 6mg/ml for perflacine and cefuroxine respectively. Extracts in 1% HCl and ethanol however, showed antimicrobial activity against the gram positive and negative organisms investigated, while extracts in water was only active against Escherichia coli and S. aureus [29].

The seed and pulp of papaya was shown to be bacteriostatic against several enteropathogens such as Bacillus subtilis, Enterobacter cloacae, Escherichia coli, salmonella typhi, Staphylococcus aureus, Proteus Vulgaris, Pseudomonas aeruginosa and Klebsiella pneumonia by the agar cup plate method [30].

The in vitro antimicrobial activities of cold water and ethanolic extracts of Magnifera indica, Carica papaya and Psidium guajava leaves were investigated against clinical isolates of Salmonella typhi using the agarwell diffusion method. The ethanolic extract of carica papaya at a concentration of 0.2 g/ml of the cold water extracts showed higher antimicrobial activity compared to 0.2 g/ml concentration of the ethanol extracts [31].

Anti-oxidant

The free radical scavenging activity of the aqueous leaf extraction of Carica papaya was studied by using different anti oxidant models of screening.e.g lipid peroxide(rat brain and liver),1,1-diphenyle hydrazyl (DPPH) ,2,2-azinobis –(3-ethyle benzothiazoline -6-sulphonate) (ABTS), nitric oxide ,super oxide and hydroxyl radical model. The extract showed good dose dependent free radical scavenging activity in all the in vitro models and moderate scavenging activity showed by hydroxyl radical and anti lipid peroxidation potential, which was performed using rat liver and brain homogenate [32].

The study was conducted to compare the total antioxidant activity (TAA), total phenolic content (TPC) and total flavonoid content (TFC) from the different parts of papaya tree including their ripe and unripe fruit, seeds and the young leaves. Results showed that the highest antioxidant activity through β-carotene bleaching assay was observed in unripe fruit (90.67 ± 0.29%) followed by young leave, ripe fruit and the seed. In other hand, young leaves exhibited a significant higher scavenging effect compared to others [33].

Anti-malarial

Study was conducted to document the efficacies of mosquito repellents effect of extracts of plants, plants parts used in the experiments were dried in the shade and ground to powder. The volatile constituents of the powders were isolated by dry distillation, and the distillates used in repellency tests on A. aegypti mosquitoes. The distillates of the fruits of C. frutescens and C. papaya were effective for 2.5 hours, whilst that of C. dactylon was effective for 1.5 hour. The mixture of C. frutescens and C. papaya was effective for 4 hours, whilst that of C. frutescens and C. dactylon was effective for 3 hours. The mixture of C. papaya and C. dactylon was effective for 2.5 hours compared to that of C. papaya (2.5 hours) and C. dactylon (1.5 hours), and the mixture of all three extracts was effective for 4 hours [34].

Comparative evaluations of toxicological and antimalarial effects of Carica papaya leaves, bark of Alstonia broonai and artemisinin were carried out on rats and mice respectively. Antimalarial effects were investigated on Plasmodium berghei infected mice. The extract of C. papaya and A. broonai caused significant elevation ($p<0.05$) in serum ALP, ALT and AST activities following 14 days administration while there was no significant differences ($p>0.05$) in the activities of these enzymes following 7 days administration when compared with controls.results revealed that the extract of the leaves of C. papaya and bark of A. broonai may serve as alternatives to standard drugs in the short term chemotherapeutic management of malarial infection [35].

Antimalarial activity of the ethanol leaf extract of Carica papaya (C. papaya), blood stages of CQ-sensitive and CQ resistant strains against Plasmodium falciparum (P. falciparum) as target species. The highest larval mortality in the ethanol leaf extract of C. papaya against the 1st to 4th instars larvae and pupae values of LC50= 3.65%, 4.28%, 5.41%, 6.70%, and 7.50%, respectively. The LC90 values of

9.61%, 11.75%, 13.53%, 16.36%, and 16.92%, respectively. Plant extracts showed moderate to good antiparasitic effects [36].

Anti-fungal

Antifungal potency of leaf extracts of Carica papaya on fungal pathogens implicated in soft rot of post-harvest yam was evaluated. The cup-plate agar method was used to determine the inhibition zone diameters of cold and hot ethanolic leaf extracts of Carica papaya on fungal pathogens implicated in soft rot of yam, namely; Rhizopus nigricans and Mucor circinelloides. Cold extracts showed higher zones of growth inhibition (effects) than hot extracts for each of the concentrations tested, there was no significant difference ($p>0.05$) between them; hot extract showed no antifungal effect on Mucor circinelloides. For the cold extract, there was no significant difference ($p>0.05$) in the zones of growth inhibition between Rhizopus nigricans and Mucor circinelloides, while significant difference ($p<0.05$) between their zones of growth inhibition was noticed for the hot extracts [37].

Effect of extracts from Carica papaya Linn., (seed and papain) on mycelial reduction of the most occurring fungal pathogen causing pawpaw fruit rot were investigated. Different fungi isolated were Rhizopus sp, Aspergillus sp and Mucor sp. The aqueous seed extract and papain exhibited remarkable mycelia inhibition with mean zones of inhibitions between (0.23 - 1.73 mm) [38].

Study on two ways of Carica papaya leaf extract preparations i.e. crushed and boiled were tested for their anti-fungal activity against 6 saprophytic fungi penicillium sp., Aspergilus flavus, aspergillus niger, fusarium sp, rhizopus and helminthosporum, 5 dermatophytic fungi microsporum canis, microsporum gypseum, trichophyton rubrum, trichophyton mentagrophytes, trichophyton tonsurans and 6 yeasts including candida albicans, candida albicans ATCC 0383, Saccharomyces cerevisiae, candida galbrata, candida tropicalis, candida kruzei. The activity was found against majority of fungi but was much better in case of crushed leaf extract [39].

From study, the antifungal medicinal properties of Carica papaya, the effects of different concentrations of alcoholic extract of Carica papaya (root, shoot and seed) on the radial growth of plant against the pathogenic fungi viz. Aspergillus niger, Aspergillus flavus, Candida albicans and Microsporum fulvum. That with the increase in concentrations the rate of growth inhibition also increases. Observation further shows that like root extract growth is also inhibited in the presence of shoot and seed alcoholic extract under culture medium. Further shows that the growth of these fungi inhibits more in presence of higher concentrations as compared to lower concentrations of extract [40].

Anti-ulcer

Gastro protective effects of aqueous Carica papaya seed extract on ethanol induced gastric ulcer were investigated in 32 male rats. The results showed that the extract protected the gastric mucosa against ethanol effect. C. papaya extract significantly reduced the gastric juice volume and gastric acidity ($p<0.05$) in dose dependent manner when compared with the control. The percentage ulcer inhibition was significantly high ($p<0.05$) in rats treated with the extract when compared with the control and the effect is similar to that of rats treated with cimetidine [41].

Aqueous extract of unripe Carica papaya fruit (AEUCPF) was investigated for its anti-ulcer, mucus secretion, anti-acid secretory and pepsin binding effects in rats. Ethanol/HCl and Indomethacin were used to induce ulcers while acid and mucus secretion was measured in ulcerated and treated animals. The results showed that higher doses of the extract significantly ($p<0.05$) reduced the ulcer index from 3.6± 0.24 (control) – to 0.70 ± 0.37 (4.5ml/Kg) in the ethanol induced ulcer. The extract also produced similar effects in the indomethacin induced ulcer and in both cases the gastric acidity was significantly reduced [42].

Anti-HIV

From study, The evaluation of anti-HIV-1 effect of Carica papaya aerial parts polar extracts, the methanol and aqueous extracts of Carica papaya were tested for their anti-HIV-1

activity using the syncytia formation assay. Methanol and aqueous extracts of Carica papaya aerial parts showed activity as anti-HIV-1 agents, both of the extracts Therapeutic index (TI) of 5.51 and 7.13 compared with the standard drug [43].

Anti-fertility

The effects of ethanol extract of Spondias mombin leaf on male rats' fertility were investigated. The extract was orally administered with 250 and 500mg/kg doses for 8 weeks. There was significant decrease in testicular and epididymal weight in the treated animals compared to the control. Histomorphology of the testis showed distortion in the arrangement of seminiferous tubules, loose germinal epithelium, low number of germ cells and Sertoli cells. Tubular sizes of epididymis were reduced with vacuolation and decreased sperm. The serum level of testosterone was significantly decreased ($p<0.05$) at 500mg/kg compared to control. We conclude that Spondias mombin leaf extract can suppress the process of spermatogenesis which can lead to infertility in laboratory animals [44].

From the investigation, the effect of Carica papaya seed extract on steroidogenesis, the cholesterol levels in testes were significantly decreased by the Carica papaya seed extraction indicating decreased mobilization towards androgenesis which leads to decreased steroidogenesis and thereby inhibition of spermatogenesis in testes. It is noticed that the liver cholesterol was significantly enhanced with reduced blood cholesterol. The lowering of the 3β- HSD and 17β-HSD activity levels in the testes suggest the antifertility agents interfere with steroid hormone biosynthesis, which ultimately result in impaired spermatogenesis and infertility [45].

Another study on the antifertility activity and reversibility of ethanol extract of C. papaya seeds in sexually matured male Wistar rats, where 30 adult males and 60 female Wistar rats weighing between 180 and 220 g were used for the study. The results showed normal pregnancy outcome in the females paired with the control group, reduced and zero pregnancy outcome in the females paired with the 100 and 250 mg/kg groups respectively after 90-day administration of the extract. After 90 days of discontinued administration of extract, normal pregnancy outcome were recorded in both the control and treated groups. The result of the histopathological analysis showed a moderate and highly depleted germinal epithelium in the 100 and 250 mg/kg groups respectively after 90 day administration of the extract. The germinal epithelium seen in both the control and the experimental groups were normal after 90 days discontinued extract administration. The study concludes that ethanol extract of C. papaya seeds induces reversible male contraception in Wistar rats [46].

From study, the effects of carica papaya leaf methanol extract on frtiliy in male Wister rats using sperm counts and percentage of defective sperm cells as markers. Thirty two male Wister rats were divided into 4 groups and treated orally with 100, 200 and 400 mg/kg B.W., respectively with the extract. Result showed CPMLE significantly produced dose dependent decrease in sperm counts and increased the percentage of defective sperm cells and from further results it concluded that CPLME can produce some defects to fertility and may be used to control birth rate [47].

Anti-diabetic

Study on hypoglycemic effect of the aqueous extract of C. papaya leaves in diabetic rats, where Diabetes was induced in rats by intraperitoneal administration of 60 mg/kg of streptozotocin (STZ). The aqueous extract of Carica papaya (0.75 g and 1.5 g/100 mL) significantly decreased blood glucose levels ($p<0.05$) in diabetic rats. It also decreased cholesterol, triacylglycerol and amino-transferases blood levels. Low plasma insulin levels did not change after treatment in diabetic rats [48].

Study on the long term (24 weeks) anti-diabetic, anti-hyperlipidaemic and antiatherogenic effects of aqueous leaf extract of Carica papaya in streptozotocin (STZ) diabetic rats. Results showed, Treatment of STZ diabetic rats with C. papaya leaf extract produced significant ($P<.05$) reductions in FBS from week 2 of treatment. Normoglycaemia was attained in week 8 and sustained till week 24. Significant ($P<.05$)

reductions in serum total cholesterol and LDL-cholesterol concentrations were also observed for most of the points monitored while HDL-cholesterol was significantly (P<.05) increased. The high AI and CRI caused by STZ diabetes was significantly (P<.05) reduced in the C. papaya treated diabetic rats [49].

The study investigated the interacting effects of co-administration of Carica papaya leaf extract on the hypoglycemic activity of metformin and glimepiride in an animal model. Results showed, the Extract of Carica papaya at 5.0 mg/kg produced significant blood glucose reduction with no significant reduction at the higher dose of 10 mg/kg (p>0.05). Changing nature from "low" (Carica papaya extract) to "high" (glimepiride or metformin) did not significantly change hypoglycemic activity. Generally, the ranking of the interacting effects was ND>CD>>NC for glimepiride/extract, and CD>ND>NC for metformin/extract. Administration of higher dose of the extract led to significant (p<0.01) increase in onset of activity of glimepiride. The onset of activity of metformin was not affected, but a significant lowering (p<0.05) of blood glucose was observed at 24 hr with all combinations of extract and metformin [50].

Study on crude extract of Carica papaya seeds was prepared in boiling water and the aqueous extract was dried. At a dose of 100 mg/kg, 200mg/kg the extract was given to Male Sprague- Dawley rats for 14 days to evaluate the anti hyperglycemic and anti hyperlipidaemic activity in Streptozotocin - Nicotinamide induced diabetic rats. Dosage of 100mg/kg and 200mg/kg of the extract significantly (P<0.001, P< 0.01) decreased blood glucose levels and the decrease was found to be dose dependent. SGOT, SGPT levels were decreased (P<0.01, P<0.05). Lipid profile was also decreased significantly (P<0.01, P<0.05) [51].

Anti-hypertensive

Ethanolic extract of Carica papaya L. root bark powder (Family: Caricaceae) was evaluated for its antihypertensive activity in renal artery occluded hypertensive rats. Male Wistar rats (180-200g) were pretreated with ethanolic extract of Carica papaya L. root bark for 6 weeks. Hypertension was induced in animals by clamping the renal artery with renal bulldog clamp for 4 h. Ischemia of the kidneys causes elevation of blood pressure by activation of the renin-angiotensin system. Elevated blood pressure of the animals was significantly (P<0.001) decreased by the ethanolic extract of Carica papaya Linn. [52].

CONCLUSION

Papaya is well recognized for its admirable nutritional and medicinal properties all over the world. At the present time, papaya is considered as a Nutraceutical fruit due to its assorted medicinal properties. Quit a remarkable amount of work has been done on the pharmacological activity and thus extensive investigation on its pharmacodynamics, kinetics and proper standardization and clinical trials is desired to make use of their therapeutic effectiveness to conflict a array of diseases.

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