**Carica papaya** Linn: A Potential source for various health problems

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Received on: 15-01-2010; Revised on: 16-03-2010; Accepted on:19-04-2010

**ABSTRACT**

*Carica papaya* is cultivated for its fruits; it is flavored by the people of the tropics, as breakfast and as ingredients in jellies, preserves or cooked in various ways. Papain the proteolytic enzyme has a wealth of industrial uses. It is used for meat tenderizers and chewing gums. In traditional practices juice of plants is used for curing warts, cancer, and tumors. Recent researches in different parts of the world have shown that *C. papaya* has the great potential against a number of health problems. *C. papaya* preparations can be efficiently used in tissue burn, microbial/helminthic infection. It can be used as antioxidant, immunomodulatory, hypoglycemic and hypolipidemic effects. Instead of these effects, it can be also used as insecticidal/molluscicidal activity against various pests. The present review highlights the some important pharmacological uses of papaya plants in ancient as well as recent time.

**Keywords:** *Carica papaya*, papain, hypoglycemic and hypolipidemic, antioxidant, insecticidal, molluscicidal.

**INTRODUCTION**

*Carica papaya* Linn. is a monoecious, dioecious or hermaphrodite tree; it belongs to the family Caricaceae [1,2]. It is widely cultivated throughout world and is used as food and traditional medicine, particularly as an antiseptic and contraceptive. This plant contains specialized cells (laticifers) dispersed throughout most plant tissues that secrete a substance known as 'latex'[3]. Latex is a complex mixture of chemical compounds with diverse chemical activities collectively; these compounds are thought to be involved in defense of the plant against a number of pests [3]. The use of papaya leaf, fruit and root extracts as traditional medicine [4,5], meat tenderizers and chewing gums [6] and the complex chemical composition of papaya latex, suggests its potential for treatment of various health problems of human and other organism. Before, dealing with different biological events, we should discuss the chemical composition of different parts of the papaya plants.

**CHEMICAL CONSTITUENTS**

*Carica papaya* seeds possess moisture 71.89, protein 8.4, carbohydrate 9.44, ash 1.47%, Fatty oil- lauric 0.13, myristic 0.16, palmitic 15.13, stearic 3.61, arachidic 0.87, behenic 0.22, oleic 71.60, linoleic 7.68, linolenic 0.6%, Phospholipids- phosphatidylcholine, phosphatidylcholine, cardiolipin [7]. Other compounds present in seeds are carpaine, benzylisothiocyanate, benzylglucosinolate, glucotropaeolin, benzylthiourea, henriciacontane, beta-sitosterol, carcin (identical with sinigrin) and an enzyme myrosin [7]. Benzyl isothiocyanate is the main bioactive compound responsible for the anthelmintic activity of papaya seeds [7-12].

Latex is a complex mixture of chemical compounds with diverse chemical activities. Cysteine proteinases may constitute as much as 80% of the enzyme fraction in papaya latex [3]. The most well studied proteinases from papaya are papain, chymopapain, caricain and glycyl endopeptidase. Papain occurs in all parts of the tree except the root [7]. It protects the tree from many herbivorous insects and pests[13]. It is widely used in both the food manufacturing and pharmaceutical industries. Sensitization to papain among workers in these industries is well known[14, 15].

**BIOLOGICAL EFFECTS OF CARICA PAPAYA**

Mikhal’chik [16] and Gurung and Basnet [17] demonstrated that treatment with the phytopreparation from papaya accelerated wound healing and reduced the severity of local inflammation in rats with burn wounds. The effect of this phytopreparation can be related to an increase in the effectiveness of intracellular bacterial killing by tissue phagocytes due to the inhibition of bacterial catalase. Antioxidant activity of the preparation decreases the risk of oxidative damage to tissues. *Carica papaya* is used in The Gambia at the Royal Victoria Hospital, Banjul in the Pediatric Unit as the major component of burns dressings, where it is well tolerated by the children. Cheap and widely available, the pulp of the papaya fruit is mashed and applied daily to full thickness on infected burns. It appears to be effective in desloughing necrotic tissue, preventing burn wound infection and providing a granulating wound suitable for the application of a split thickness skin graft. Possible mechanisms of action include the activity of proteolytic enzymes chymopapain and papain, as well as antimicrobial activity[18]. Papaya is widely used by nurses...
as a form of dressing for chronic skin ulcers in Jamaica. The topical application of the unripe fruit promoted desloughing, granulation and healing and reduced odour in chronic skin ulcers[19]. The people of Ngada also use fruits of papaya (Carica papaya L.) for wound treatment[20].

Rahmat [21] have reported that consumption of C. papaya (400 g/day) reduces the oxidative stress and alters lipid profile. Thus, it could reduce the risk of disease caused by free radical activities and high cholesterol in blood [22]. The ethanolic and aqueous extracts of C. papaya show remarkable hepatoprotective activity against CCl4 induced hepatotoxicity [23].

Preliminary study on the hypoglycemic effect of C. papaya seed demonstrates that it significantly lowers the blood glucose level in Wister rats [22]. Diabetes complications, especially late (chronic) ones, are the main reasons of invalidity and early mortality. The most threatening diabetes complications are vascular and metabolic complications (diabetic neuropathy, angiopathy, cataract, glaucoma, optic neuropathy, retinopathy, diabetic nephropathy). Good diabetes control is very important, because in early stages these changes are reversible. In order to decrease the number of diabetes complications and to postpone their development, Savickiene[24] recommended the use of biologic active components and plants. The most important biologic active substances for this purpose are vitamins and minerals, proteins, polysaccharides, lectins, saponins and flavonoids. According the scientific data, the mostly used plants are: Ginkgo biloba, Allium sativum, Silybum marianum, Panax ginseng, Carica papaya, Vaccinium myrtillus, Phaseolus vulgaris. Some of them are proposed for treatment of symptoms related to venous and lymphatic vessel insufficiency, for the prophylaxis and treatment of liver damage caused by metabolic toxins, in chronic degenerative liver conditions, for the therapy of digestive disorders, to increase in the specific way the resistance of the organism to various environmental influences and to stabilize membranes through antioxidant and radical scavenging actions.Carica papaya skin extract may be used as an alternative to enzyme pepsin for digestion of swamp eel viscerca for harvesting Gnathostoma spinigerum third-stage larvae[25]. Okeniyi[26] reported that air-dried C. papaya seeds are efficacious in treating human intestinal parasites and without significant side effects.

Kamaruzzaman [27] determined the chemical composition of dried papaya (Carica papaya) skin (DPS) and investigated its potential as a dietary ingredient for broiler chickens at dietary concentrations of 0, 40, 80 and 120g/kg. DPS was found to give similar food consumption, food conversion efficiency, survivability and meat yields (except male liver weight) to a control diet when used up to 120 g/kg of diet. Weight gain tended to increase with dietary concentration of DPS up to 80 g/kg. It was concluded that DPS could safely be used up to 120 g/kg in the diet of broiler chickens.

Ananthelmintic properties

In in vitro Carica papaya seeds show potential ananthelmintic properties against egg, infective larvae and adult worms of parasitic nematode, Trichostrongylus colubriformis [11]. Benzyl isothiocyanate is the chief or sole ananthelmintic in papaya seed extracts [8]. Satrija [28] reported the ananthelmintic activity of papaya latex against Heligmosomoides polygyrus infections in mice. Further, ananthelmintic efficacy of cysteine proteinases from papaya and other plants was investigated in vitro using the rodent gastrointestinal nematode Heligmosomoides polygyrus. Within a 2h incubation period, cysteine proteinases, caused marked damage to the cuticle of Heligmosomoides polygyrus adult male and female worms, reflected in the loss of surface cuticular layers. The mechanism of action of these plant enzymes (i.e. an attack on the protective cuticle of the worm) suggests that resistance would be slow to develop in the field. The efficacy and mode of action make plant cysteine proteinases potential candidates for a novel class of anthelmintics urgently required for the treatment of human and domestic livestock [29]. Okeniyi[26] observed that C. papaya dried seeds have proven ananthelmintic and antiamaebic activities. According them air-dried C. papaya seeds are efficacious in treating human intestinal parasites.

Antiprotozoan activity

Ekanem [30] investigated the activity of petroleum-ether extract of seeds of C. papaya against the ciliate protozoan Ichthyophthirius multifiliis in vivo and in vitro conditions. Goldfish (Carassius auratus auratus) infected with the parasites were immersed for 96h in baths with C. papaya extract. There was a 90% reduction in numbers of I. multifiliis on fish after treatment in bath plant extract at 200 mg/l compared to untreated control. Consequently, parasite-induced fish mortality was reduced significantly. In vitro tests led to a 100% mortality of I. multifiliis in 200 mg/l of C. papaya extract after 6h. The plant extracts have potential antiprotozoan activity for effective control of I. multifiliis.

Antibacterial activity

Emeruwa [31] and Dawkins [32] have reported that Carica papaya fruit and seed extracts contain antibacterial activity that could be useful in treating chronic skin ulcers to promote healing. All the extracts of C. papaya fruit and seed have very significant antibacterial activity against Staphylococcus aureus, Bacillus cereus, Escherichia coli, Pseudomonas aeruginosa, Salmonella typhi, Proteus vulgaris, Klebsiella pneumoniae and Shigella flexneri [31].

Nkwo-Akenji [33] evaluated the effects of methanol extracts of plant parts commonly used in Cameroon for the treatment of typhoid fever for antibacterial activity against Salmonella typhi, S. paratyphi and S. typhimurium. The formulations used were: 1) Formula A comprising Cymbogogon citratus leaves, Carica papaya leaves, and Zea mays silk. 2) Formula B comprising C. papaya roots, Mangifera indica leaves, Citrus limon fruit and C. citratus leaves. 3) C. papaya leaves. 4) Emilia coccinea whole plant. 5) Comelina bengalensis leaves. 6) Telfaria occidentalis leaves. 7) Gossypium arboreum whole plant. Antimicrobial activity was tested using the minimum inhibitory concentration (MIC) and the minimum bactericidal concentration (MBC) assays. Generally, Formulation A elicited inhibitory activity at a lower range of 0.02 to 0.06 mg/ml. Similarly, Formulation B elicited bacterial activity at the lowest range of 0.06 to 0.25 mg/ml. C. bengalensis leaves on the other hand, showed the lowest activity with a concentration range of 0.132 to 2.0 mg/ml and 1 to 4 mg/ml in MIC and MBC assays, respectively. S. paratyphi was most sensitive to the formulations (concentration range of 0.02 to 1 mg/ml in both MIC and MBC assays) while S. typhimurium was the least sensitive and concentrations of up to 4 mg/ml were required to be bactericidal.
Antifungal activity

Giordani [34] have reported the antifungal activity of Carica papaya latex sap against Candida albicans. Carica papaya latex sap inhibits the growth of Candida albicans when added to a culture during the exponential growth phase. A mixture of Carica papaya latex (0.41 mg protein/ml) and fluconazole (2 µg/ml) also showed a synergistic action on the inhibition of C. albicans growth [35].

Antioxidant activity

Mehdipour [36] explored the toxicological and antioxidant potential of dried Carica papaya juice in vitro and in vivo. In vivo examination was performed after oral administration of dried papaya juice to rats for 2 weeks at doses of 100, 200 and 400 mg/kg. The acute toxicity test LD₅₀ demonstrated that papaya juice is not lethal up to a dose of 1500 mg/kg after oral administration and thus is considered nontoxic. In treated groups, no sign of toxicity was observed. In vitro evaluation of the antioxidant effects of papaya showed that the highest antioxidant activity 80% was observed with a concentration of 17.6 mg/ml. Blood lipid peroxidation levels decreased significantly after administration of all doses of papaya juice (100, 200, 400 mg/kg/day) to 35.5, 39.5 and 40.86% of the control, respectively, compared with a value of 28.8% for vitamin E. The blood total antioxidant power was increased significantly by all doses of papaya juice (100, 200, 400 mg/kg/day) to 11.11, 23.58 and 23.14% of the control, respectively. The value for vitamin E was 18.44%. This study indicates the safety and antioxidative stress potential of Carica papaya juice, which was found to be comparable to the standard antioxidant compound alpha-tocopherol. Nakamura [12] reported that hexane extract of Carica papaya seed homogenate is highly effective in inhibitory superoxide generation and apoptosis in H2-60 cells. Olagunju [37] observed that the aqueous seed extract of the unripe mature fruits of Carica papaya has nontoxic properties. It is due to its antioxidant and/or oxidative free radical scavenging activities.

Immunomodulatory activity of Carica papaya

Carica papaya seed extract is currently being marketed as a nutritional supplement with purported ability “to rejuvenate the body condition and to increase energy.” The product claims to improve immunity against common infection and body functioning. Mojica-Hensch [38] analyzes the chemical constituents of the Carica seed extract and determine the potential immunomodulatory properties of the different bioactive fractions. These immuno modulatory activities of crude Carica seed extract and its bioactive fractions were examined in vitro using lymphocyte proliferation assays and complement-mediated hemolytic assay. Three major observations were made in this study: (1) the crude Carica seed extract and two other bioactive fractions significantly enhanced the phytohemagglutinin responsiveness of lymphocytes; (2) none of the Carica seed extract was able to protect the lymphocytes from the toxic effects of chromium; and (3) some of the bioactive fractions of Carica seed extract were able to significantly inhibit the classical complement-mediated hemolytic pathway. These findings provide evidence for immunostimulatory and anti-inflammatory actions of Carica seed extract. No single compound is likely responsible for these activities. Rimbach [39] observed that fermented papaya preparation is a macrophage activator which augments nitric oxide synthesis and tumor necrosis factor-alpha.

Marotta [40] have studied the effect of a novel antioxidant/ immunomodulator (alpha-tocopherol or fermented papaya preparation) in patients with hepatitis C virus (HCV) - related cirrhosis. The data obtained from this study suggest a potential supportive role of fermented papaya preparation as antioxidants/immunomodulators in HCV patients.

Insecticidal and larvicidal activity

Konno [13] found that papain, a cysteine protease in latex of the Papaya tree (Carica papaya, Caricaceae), is a crucial factor in the defense of the papaya tree against lepidopteran larvae such as oligophagous Samia ricini (Saturniidae) and two notorious polyphagous pests, Mamestra brassicae (Noctuidae) and Spodoptera litura (Noctuidae). Leaves of a number of laticiferous plants, including papaya and a wild fig, Ficus virgata (Moraceae), showed strong toxicity and growth inhibition against lepidopteran larvae; though no apparent toxic factors from these species have been reported. When the latex was washed off, the leaves of these lactiferous plants lost toxicity. Latexes of both papaya and the wild fig were rich in cysteine-protease activity. E-64, a cysteine protease-specific inhibitor, completely deprived the toxicity of leaves when painted on the surface of papaya and fig leaves. Cysteine proteases, such as papain, ficin, and bromelain, all showed toxicity. The results suggest that plant latex and the proteins in it, cysteine proteases in particular, provide plants with a general defense mechanism against herbivorous insects. Latex from unripe fruits of Carica papaya shows mosquito larvicidal properties [41].

Molluscicidal activity

C. papaya seed and latex are potential source of botanical molluscicides. Carica papaya lyophilized latex is more effective than seeds against L. acuminata. The molluscicidal activity of C. papaya seed and latex may be due to the presence of papain. Papain occurs in all parts of the tree except the root [7]. Lyophilized latex from the skin of unripe fruits and pure papain show about similar toxicity against L. acuminata at all exposure period whereas column purified fraction of Carica papaya seed shows lower toxicity than lyophilized latex. It is due to the presence of high concentration of papain in C. papaya latex than seed [7,42].

A comparison of the molluscicidal activity of C. papaya seed and lyophilized latex with synthetic molluscicides clearly demonstrate that they are more potent. Thus the 96h LC₅₀ of column purified fraction of C. papaya seed (7.06 mg/l) and lyophilized latex (8.38 mg/l) [42], against L. acuminata was lower than those of synthetic molluscicides: aldicarb (11.50 mg/l), phorate (15.0 mg/l) and formotion (8.56 mg/l) [43,44]. 96h LC₅₀ of crude powder of C. papaya seed (61.56 mg/l) and lyophilized latex (8.38 mg/l) against L. acuminata was lower than the crude powder of Abrus precatorius seed (93.83 mg/l), Punica granatum bark (62.62 mg/l), Cana indica root (359.02 mg/l) and Lawsonia inermis seed (125.84 mg/l) [45-48].

Male contraceptive / male anti-fertility property

Lohiya [49,50] have suggested that Carica papaya seeds may be a safe approach to male anti-fertility. Pathak [51] reported that oral administration of benzene chromatographic fraction of the chlo-
roform extract of *C. papaya* seeds produce sterility due to inhibition of sperm motility in rats. Kusemiju [52] studied the effect of crude extract of *C. papaya* on the seminiferous tubules of male Sprague-Dawley rats. It was found that complete loss of fertility is attributed to decline in sperm motility and alteration in their morphology and suggest that the aqueous extracts of *C. papaya* bark is safe and could serve as an effective male contraceptive in animals.

Udoh [53] studied the effects of oral administration of *C. papaya* seed extract on the morphology of pituitary, testis and sex accessory glands of sexually mature male Wistar rats. After 1 and 8 weeks of treatment, the microscopic examination of the sections of pituitary gonadotrophs (FSH and LH cells) treated with 200 mg/kg of *C. papaya* extract showed pronounced hypotrophy, while section of rats treated with 50 mg/kg showed mild hypertrophy and hyperplasic. Whereas the testis of rats treated with *C. papaya* extract at 50 and 200 mg/kg revealed gradual degeneration of germ cells, sertoli cells and leydig cells as well as germinal epithelium. However, tubules of epididymis of rats treated with extract, 200 mg/kg, appeared empty indicating the degeneration of sperm cells in the lumina. The sections of prostate glands of rats treated with 200 mg/kg extract showed coagulation of secretion in the lumina as well as empty tubules with cell debris, while the effect was reduced in rats treated with 50 mg/kg. The seminal vesicles showed progressive collapse and shrinkage of villi. These results suggest that *C. papaya* extract interfered with the pituitary-gonadal axis to influence male reproductive functions, which confirmed its antifertility property.

Verma and Chinoy [54] evaluated the administration of *Carica papaya* seed extract on the contractility of cauda epididymal tubules in male rats. Adult male albino rats were administered intramuscularly papaya seed extract at a dose of 0.5 mg/kg/day for 7 days. Animals were killed, cauda epididymal tubules of 5 cm length were isolated and the contractile response to different concentrations of adrenalin (1-500 microg/25mL) was examined. Papaya seed extract brought about a significant decrease in the contractile response of epididymal tubules as compared with the control. After three months of papaya withdrawal, a nearly normal pattern of contraction was regained. Thus papaya seed treatment reversibly reduces the contractile response of cauda epididymal tubules.

Manivannan [55] tested the benzene chromatographic fraction of the chloroform extract of *Carica papaya* seed at a dose of 10 mg/rat/day for 150 days, which has shown a total inhibition of motility, reduced sperm count and infertility, to define the mode of action at the subcellular level in the testis and epididymis. The ultrastructure of the testis of the treated animals revealed no appreciable changes in the subcellular characteristics. The mechanism of protein synthesis as well as steroidogenesis were evident in the sertoli cells while the spermatogonia, spermatocytes and spermatidis, both round and elongated, depicted a prominent nucleus, distinct nuclear membrane and cytoplasmic characteristics indicating normal germ cell differentiation. The principal cells of the cauda epididymis were characterized by the presence of well-defined rough endoplasmic reticulum, mitochondria, Golgi bodies and secretory granules, suggesting active secretory functions. The absorptive function of the cauda epididymis was evidenced by the presence of numerous vesicles and multivesicular bodies adjacent to stereocilia. It is concluded that the inhibition of sperm motility by the drug could be due to other epididymal factors rather than the subcellular characteristics of testis and epididymis. Mansurah [56] reported that unfermented extract of *C. papaya* seeds, at a higher dose of 1500mg/kg has contraceptive effects in female Wister rats, whereas, fermented seeds of *C. papaya* does not have contraceptive ability and may be safe for human consumption.

**Effect of Carica papaya consumption in pregnancy**

Schmidt [57] reported that papain present in *Carica papaya* latex shows anti-implantation activity, increased postimplantation loss and embryotoxicity when administered orally to Wister rats. Oderinde [58] conducted experiments to investigate the abortifacient potential of aqueous extract of *Carica papaya* (Linn) seeds in female Sprague-Dawley rats. Oral doses of 100 and 800 mg/kg body weight were administered once a day on days 1-10 post-coitum. No significant differences in total body weight were found in foetuses exposed to these regimes. However, in the group treated with 100 mg/kg body weight, there was a significant increase (p < 0.05) in the implantation sites and foetal weight was significantly decreased (p < 0.05) compared to the controls. No dead or malformed foetuses were found. However, in the group treated with 800 mg/kg body weight, there was obvious vaginal bleeding but no treatment related increase in implantation sites compared with control. There was however, complete resorption of about 30% of the foetuses. The surviving foetuses were stunted when compared with the control but were without any external malformations. The results of the present investigations lead to the clear conclusion that low dose aqueous crude extract of *Carica papaya* seeds does not adversely affect prenatal development. The altered toxicological profile indicates that the abortifacient property is a high dose side effect. The results indicate that *Carica papaya* toxicity can adversely affect the foetus.

Adebiyi [59] evaluated the safety of *Carica papaya* consumption in pregnancy with reference to its common avoidance during pregnancy in some parts of Asia using controlled in vivo and in vitro pharmacological methods. Ripe papaya (*Carica papaya*) blend (500 ml/l water) was freely given to four groups of Sprague-Dawley rats at different stages of gestation (days 1-5, 6-11, 12-17 and 1-20). The control group received water. The effect of ripe papaya juice and crude papaya latex on pregnant and non-pregnant rats’ uteri was also evaluated using standard isolated-organ-bath methods. The daily volumes (ml) of ripe papaya blend consumed by the treated group were significantly (P<0.05) more than water consumed by the control. There was no significant difference in the number of implantation sites and viable fetuses in the rats given ripe papaya relative to the control. No sign of foetal or maternal toxicity was observed in all the groups. In the in vitro study, ripe papaya juice (0.1-0.8 ml) did not show any significant contractile effect on uterine smooth muscles isolated from pregnant and non-pregnant rats’ uterus was also evaluated using standard isolated-organ-bath methods. The daily volumes (ml) of ripe papaya blend consumed by the treated group were significantly (P<0.05) more than water consumed by the control. There was no significant difference in the number of implantation sites and viable fetuses in the rats given ripe papaya relative to the control. No sign of foetal or maternal toxicity was observed in all the groups. In the in vitro study, ripe papaya juice (0.1-0.8 ml) did not show any significant contractile effect on uterine smooth muscles isolated from pregnant and non-pregnant rats; conversely, crude papaya latex (0.1-3.2 mg/ml) induced spasmodic contraction of the uterine muscles similar to oxytocin (1-64 mU/ml) and prostaglandin F2α (0.028-1.81 microm). The response of the isolated rat uterine smooth muscles to 0.2 mg crude papaya latex/ml was comparable to 0.23 microm prostaglandin F2α and 32 mU oxytocin/ml. In the 18-19 d pregnant rat uterus, the contractile effect of crude papaya latex was characterized by tetanic spasms. The results of the present study suggest that normal consumption of ripe papaya during pregnancy may not pose any significant danger. However, the unripe or semi-ripe papaya (which contains high concentration of the latex that produces marked uterine contractions) could be unsafe in pregnancy.
Though evaluation of potentially toxic agents often relies on animal experimental results to predict risk in human, further studies will be necessary to ascertain the ultimate risk of unripe papaya-semi-ripe papaya consumption during pregnancy in human. Further Adebiyi [60] reported that 80% ethanol extracted papaya seed (EEPS) caused concentration-dependent tocolysis of uterine strips isolated from gravid and non-gravid rats. Prostaglandin F₂ and oxytocin-induced contractions of the isolated rat uterus were also inhibited in a concentration-dependent fashion by EEPS. Recoveries of the uterine activity after EEPS-induced uterine quiescence were very weak. Higher concentration of EEPS caused prompt uterine quiescence, which was also significantly irreversible. Pre-incubation of the rat uterus in Ringer Locke solution containing 10 mg/ml of EEPS for 1 hour prior to suspension in tissue baths led to significant depression of the spontaneous and KCl (60 mM)-induced uterine contractions relative to the solvent control (P < 0.05). Cross sections of EEPS-pre-treated non-gravid rat uterus examined under light microscope revealed degeneration of the endometrium and myometrium with obvious cytoplasmic vacuolation indicating that EEPS could have direct toxic effect on the uterine tissues. Previous workers have reported benzyl isothiocyanate (BITC) as the main bioactive and anthelmintic compound in different extracts of papaya seeds. Using electron impact ionization methods, the presence of BITC in EEPS was also shown in this study. Mass spectra of both EEPS and standard BITC showed a base peak of benzyl/tropylum ion at m/z 91 and the molecular ion peak of BITC (m/z 149). It has been demonstrated that BITC-induced functional and morphological derangement of isolated uterus. A high concentration, EEPS is capable of causing irreversible uterine tocolysis probably due to the damaging effect of BITC (its chief phytochemical) on the myometrium [59, 60].

**Vasodilatory effect of Carica papaya**

Runnie [61] investigated the vasodilatory actions of nine edible tropical plant extracts. *Ipomoea batatas* (sweet potato leaf), *Piper betle* (betel leaf), *Anacardium occidentale* (cashew leaf), *Gynandropis gynandra* (mamam leaf), *Carica papaya* (papaya leaf), and *Mentha arvensis* (mint leaf) extracts exhibited more than 50% relaxing effect on aortic ring preparations. While *Piper betle* and *Cymbopogon citratus* (lemongrass stalk) showed comparable vasorelaxation on isolated perfused mesenteric artery preparation. The vasodilatory effect on the aortic ring preparations were mainly endothelium-dependent, and mediated by nitric oxide as supported by the inhibition of action in the presence of N(omega)-nitro-L-arginine, an nitric oxide synthases inhibitor, or by the removal of endothelium. In contrast, vasodilatory actions in resistance vessels (perfused mesenteric vascular beds) appear to involve several biochemical mediators, including nitric oxide, prostanoids, and endothelium-dependent hyperpolarizing factors. Total phenolic contents and antioxidant capacities varied among different extracts and found to be independent of vascular relaxation effects. This study demonstrates that many edible plants common in Asian diets possess potential health benefits, affording protection at the vascular endothelial level.

To investigate their potentially toxic effects on mammalian vascular smooth muscle, Wilson [9] tested the effects of pentane extracts of papaya seeds and the chief active ingredient in the extracts, benzyl isothiocyanate (BITC), on the contraction of strips of dog carotid artery. BITC and the papaya seed extract caused relaxation when added to tissue strips that had been pre-contracted with phenylephrine (PE). Incubation of the tissue with papaya seed extract or BITC caused inhibition of contraction when the strips were subsequently contracted with KCl or PE. This relaxation and inhibition of contraction did not appear to be endothelium-dependent, as endothelium-denuded rings showed the same degree of relaxation or inhibition of contraction in response to the preparations/drugs as those with the endothelium intact. The effects of both BITC and the extract were irreversible, i.e., the tissue did not recover to normal contractile ability after extensive washing. Exposure of the tissue to the papaya seed extract caused slower relaxation of the tissue, compared to controls, both after contraction with PE and subsequent addition of carbachol (CCh), and after contraction with KCl and then washing. Calcium imaging studies using cultured endothelial cells showed strong influxes of Ca²⁺ into the cells in response to addition of the papaya seed extract. These extracts, when present in high concentration, are cytotoxic by increasing the membrane permeability to Ca²⁺, and that the vascular effects of papaya seed extracts are consistent with the notion that BITC is the chief bio-active ingredient.

**Effect of papaya on anoxic damaged cerebral neurocytes**

Chang [62] studied the effects of papaya on the therapeutic efficacy of cerebral neurocytes following anoxic damage in vitro. The rat embryonic cerebral neurocytes were cultured with serum-free medium. Papaya was added in while anoxic damage occurred and the neurocytes were divided into four groups (group I-anoxic damage 0 mg/ml, group II-anoxic damage 0.1 mg/ml, and group III-anoxic damage 0.5 mg/ml and group IV-non-anoxic damage 0 mg/ml). At the end of the experiment, cultured neurocytes were collected and biochemical indexes were detected and, a pathological observation was made by using electron microscope. The activity of MTT in group II was significantly higher than that in the other three groups (P < 0.01). Compared with group I and IV, the level of TCHE in group II and III was increased significantly (P < 0.05), and the level of TCHE in group III was much higher than that in group II (P < 0.05). The morphological observation showed that the number of neurocytes in group I decreased, and the appearance of cell was broken, the outer limits were not clear, apophysis were thin and short, and apoptosis body can be found. In group II and III, stretched preparation of majority cells was good, the bodies of neurocytes was full-grown, the outer limits were clear, apophysis were strong, and network was dense and chromatin was partly condense, but apoptosis bodies can not be found. Thus papaya can promote the recovery of anoxic damage of rat cerebral neurocytes in structure.

It can be concluded from the above ongoing literature that *C. papaya* has the great potential against a number of health problem viz. tissue burn, bacterial/fungal/ helminthic/protozoan infection. It has antioxidant, immunomodulatory, insecticidal/ molluscidial activity. Recently it has shown some hypoglycemic as well as hypolipidemic effects in its seed preparations. It needs greater attention by scientist to make further studies regarding its efficient use in the cure of mankind.

**REFERENCES**
