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A review on medicinal properties of *Carica papaya* Linn.

Tarun Vij*, Yash Prashar

Rayat Institute of Pharmacy, Railmajra, SBS Nagar, Punjab, India

PEER REVIEW

Peer reviewer

Dr. Manjit Singh, Lala Lajpat Rai college of Pharmacy, Moga, Punjab, India.

Tel: 7696699737

E-mail: 2009manjit@gmail.com

Comments

This is a good study in which the evaluation of the various parts of the papaya was carried out by the literature review. The study includes the pharmacological activities, presence of enzymes, traditional uses and nutritional values of the plant.

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ABSTRACT

Papaya (*Carica papaya* L.) is a popular and important fruit tree in tropical and subtropical parts of the world. The fruit is consumed worldwide as fresh fruit and vegetable or used as processed product. The fruit is healthy and delicious and the whole plant parts including fruit, root, bark, peel, seeds and pulp are also known to have medicinal properties. The many benefits of papaya are owed due to high content of vitamin A, B and C, proteolytic enzymes like papain and chymopapain which have antiviral, antifungal and antibacterial properties. During the last few years, major insight has been achieved regarding the biological activity and medicinal application of papaya and now it is considered a valuable nutraceutical fruit plant. In the present review, nutritional value of the fruit and medicinal properties of its various parts have been discussed to provide collective information on this multipurpose commercial fruit crop.

KEYWORDS

Introduction, Nutritional value, Traditional and pharmacological properties

1. Introduction

Papaya is a powerhouse of nutrients and is available throughout the year. It is a rich source of three powerful antioxidant vitamin C, vitamin A and vitamin E. The minerals, magnesium and potassium, vitamin B pantothenic acid and folate and fiber. In addition to all this, it contains a digestive enzyme—papain that effectively treats causes of trauma, allergies and sports injuries. All the nutrients of papaya as a whole improve cardiovascular system, protect against heart diseases, heart attacks, strokes and prevent colon cancer. The fruit is an excellent source of beta-carotene that prevents damage caused by free radicals that may cause some forms of cancer. It is reported that it helped in the prevention of diabetic heart disease. Papaya lowers high cholesterol levels as it is a good source of fiber[1].

Papaya, *Carica papaya* (*C. papaya*) L., is one of the major fruit crops cultivated in tropical and sub-tropical zones.

Worldwide over 6.8 million tonnes of fruit were produced in 2004 on about 389 990 ha (FAO 2004). Of this volume, 47% was produced in Central and South America (mainly in Brazil), 30% in Asia and 20% in Africa. The papaya industry in Brazil is one of the world's largest that continues to show rapid growth. Do Carmo and Sousa Jr. (2003) reported on a 151% increase in total area cultivated over the past decade (16 012 ha in 1990 to 40 202 ha in 2000) and a 164% increase in the quantity produced during the same period (642 581 to 1 693 779 fruits from 1990 to 2000). During 11 years, the volume exported increased 560% from 4 071 t to 22 804 t in 2001 (SECEXMDIC 2002) and 38 760 t in 2005 (FAO 2005). Although papaya is mainly grown (>90%) and consumed in developing countries, it is fast becoming an important fruit internationally both as a fresh fruit and as processed products[2].

It is a tree reaching 3–10 m in height with the habit of a palm; the freshly stem marked by scars where leaves have

*Corresponding author: Tarun Vij, Rayat Institute of Pharmacy, Railmajra, SBS Nagar, Punjab, India.

Tel: 8054358107

E-mail: phtarunvij@gmail.com

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fallen off, is surmounted by a terminal panache of leaves on long petioles and with 5–7 lobes. Flowers fragrant, male flowers in lax many-flowered, densely pubescent cymes at the tips of the pendulous, fistular rachis; females flowers large, solitary or in few flowered racemes, different types of enzymes. Papain, vegetable pepsin present in good amount in unripe fruit is an excellent aid to digestion, which helps to digest the protein in food at acid, alkaline or neutral medium. Thus it can be prescribed for dyspeptic patients, who cannot digest the wheat protein gliadin, can tolerate it, if it is treated with crude papain. Papaya has the property of tenderizing meat. This knowledge is being put to use by cooking meat with raw papaya to make it tender and digestible^[3].

The fermented papaya fruit is a promising nutraceutical as an antioxidant. It improves the antioxidant defence in elderly patients even without any overt antioxidant deficiency state at the dose of 9 g/day orally^[4,5].

1.1. Introduction to plant profile

Plant profile of *C. papaya* is shown in Figure 1.



Figure 1. *C. papaya*: (A) papaya tree; (B) ripe fruit.

1.2. Taxonomical classification, common names and parts used

The papaya belongs to a small family–Caricaceae, having four genera in the world. The genus *Carica* Linn. is represented by four species in India, of which *C. papaya* Linna. is the most widely cultivated and best-known species. The taxonomical classification includes kingdom (Plantae), order (Brassicales), family (Caricaceae), genus (*Carica*), species (*C. papaya*).

Common names include papaya, pawpaw, papaw, papita, arand–kharpuja, papaya, papayabaum, papaia.

The parts used contain fruit, leaves and bark.

1.3. Chemical constituents

The different parts of papaya such as fruit, fruit juice, seed, root, leaves, bark, latex contain various chemical constituents, which are shown as follows:

1. Fruit–Protein, fat, fiber, carbohydrates, minerals: calcium, iron, vitamin C, thiamine, riboflavin, niacin, and carotene, amino acid, citric acid and malic acids (green fruits), volatile compounds: benzylisothiocyanate, cis and trans 2, 6–dimethyl–3,6 epoxy–7 octen–2–ol, alkaloids,

carpaine.

2. Juice–N–butyric, n–hexanoic and n–octanoic acids, lipids; myristic acid, palmitic acid, stearic acid, linolenic acid, linoleic acid, oleic acid.

3. Seed–Fatty acids, crude protein, crude fibre, papaya oil, carpaine, caricin, glucotropacolin, and an enzyme myrosin.

4. Root–Carposides and an enzyme myrossin.

5. Leaves–Alkaloids carpain, pseudocarpain, dehydrocarpaine I and II, choline, vitamin C and E, carposide.

6. Bark–Glucose, fructose, sucrose, xylitol, β –sitosterol.

7. Latex–Papain, chemopapain, peptidase A and B, lysozymes^[6,7].

2. Nutritional value of 100 g of papaya fruit

The constituents of ripe papaya contain: energy (163 kJ), protein (0.6 g), fat (0.1 g), minerals (0.5 g), fibre (0.8 g), carbohydrates (7.2 g), beta–carotene (888 μ m), total carotene (2740 μ m), sodium (3 mg), iron (0.10 g), vitamin A (1094 IU), vitamin E (0.73 mg), niacin (3 mg) and water (89%).

These nutritional values of papaya help to prevent the oxidation of cholesterol. Papaya is rich in iron and calcium; a good source of vitamin A, B and G and an excellent source of vitamin C (ascorbic acid). The extract and fruit juice of *C. papaya* contain alkaloids, glycosides, flavonoids, carbohydrates, saponins, terpenoids, steroids and tannins.

3. Parts and medicinal uses of *C. papaya*

C. papaya is a pack of enzymes. Different parts contain different enzymes: unripe fruit (papain, chymopapain), fruits (B carotene, carotenoids, cryptoxanthin, monoterpenoids, linalool), roots (carposides), seeds (papaya oil, glucosinolates, benzyl isothiocyanate), leaves (Zn, Mn, Fe, K, minerals), shoots (flavanoids, kaemferol, myricetin, minerals, Ca, Mg, Fe) and leaves (vitamin C and E, alkaloids, carpaine).

The traditional claims include various medicinal properties of the plant shown in Table 1.

4. Pharmacological properties of *C. papaya*

The plant *C. papaya* has been proved for various medicinal activities like antioxidant, anti–hypertensive, wound healing, hepatoprotective, anti–inflammatory, antimicrobial, antifungal, anti–fertility, histaminergic, diuretic, anti–amoebic, anti–tumor, anthelmintic, effect on smooth muscles, antimalarial, hypoglycemic activity, immunomodulatory activity, anti–ulcer activity, anti–sickling activity.

4.1. Antioxidant activity

The methanolic extract of unripe fruits of *C. papaya* was evaluated *in vivo* for its effect on activities of some antioxidant enzymes which includes glutathione peroxidase

Table 1Medicinal uses of *C. papaya* plant mentioned in traditional ayurvedic literature[8,9].

Parts	Medicinal uses
Ripe fruits	Carminative, diuretic, chronic diarrhea, dysentery, wounds of urinary tracts, stomachic, ringworm, sedative and tonic, bleeding piles, expectorant.
Unripe fruit	Diuretic, antibacterial activity, laxative, used in snakebite to remove poison, abortifacient.
Seeds	Carminative, anti-fertility agents in males, counter irritant, as a paste in the treatment of ringworm and psoriasis.
Roots	Anti-fungal activity, diuretic, checking irregular bleeding from uterus, piles.
Leaves	Asthma, beriberi, fever, abortion, dressing wounds (fresh leaves), antibacterial activity, jaundice, gonorrhea, urinary complaints, vermifuge.
Flower	Febrifuge, jaundice, pectoral properties.
Stem bark	STD, anti-fungal activity, jaundice, anti-haemolytic activity, sore teeth.

(GPx), glutathione transferase (GST), glutathione reductase, catalase and glucose-6-phosphate dehydrogenase in mice treated with a orally dose of 100 mg/kg. There is significant increase in the activities glutathione reductase, GST, GPx, glucose-6-phosphate dehydrogenase due to the ethyl acetate fraction. Significant decrease in GPx was observed in kidney following administration of ethyl acetate fraction. It was suggested that quercetin and β -sitosterol may be responsible for the antioxidant potential^[10].

4.2. Anti-hypertensive activity

The ethanolic extract of ripe fruit of *C. papaya* was used for the anti-hypertensive activity. The basal mean arterial blood pressure (MAP) were (93.8±4.5), (175.2±5.1), (181.3±6.2) mmHg in the normotensive, renal and DOCA-salt hypertensive animals. Both hydralazine (200 μ L/100 g, *i.v*) and ethanolic extract of unripe fruit of *C. papaya* (20 mg/kg, *i.v*) produced a significant depression of MAP in normotensive, renal and DOCA-salt hypertensive animals groups as compared to control. But the extract produced about 28% more depression of MAP than hydralazine in the hypertensive group. The study suggested that the unripe fruit of *C. papaya* had a potent anti-hypertensive activity^[11].

4.3. Wound healing activity

The aqueous extract of *C. papaya* fruit [100 mg/(kg-d) for 10 d] for wound healing property in streptozotocin-induced diabetic rats using excision and dead space wound models. The aqueous extract shows 77% reduction in the wound area when compared to 59% contraction to wound of the controls. Thus the result suggested that the aqueous extract of *C. papaya* had a potent wound healing property^[12].

4.4. Hepatoprotective activity

The aqueous and ethanol extract of dried fruit of *C. papaya* for its hepatoprotective activity in rats against CCl₄-induced hepatotoxicity in rats. The aqueous (250 mg/kg, *p.o*) and ethanol (250 mg/kg, *p.o*) extracts of *C. papaya* showed significant hepatoprotection by lowering the biochemical parameters such as SGPT, SGOT, serum bilirubin, alkaline phosphatase^[13].

4.5. Anti-inflammatory activity

The ethanolic extract of *C. papaya* leaves in rats using carrageenan induced paw oedema, cotton pallet granuloma

and formaldehyde induced arthritis models. The ulcerogenic activity of the extract was also investigated. The result showed that the extract at the dose of 25–250 mg/kg *p.o* exhibited significant reduction in the paw oedema in the carrageenan test. The extract produced slight mucosal irritation at higher doses^[14].

4.6. Antimicrobial activity

The aqueous extract of *C. papaya* leaves and roots at different concentrations (25, 50, 100, 200 mg/mL) showed antimicrobial activity against some human pathogenic bacteria using the agar diffusion method^[15].

4.7. Antifungal activity

The latex of *C. papaya* and fluconazole has synergistic action on the inhibition of *Candida albicans* growth. This synergistic effect results in partial cell wall degradation. Latex proteins appear to be responsible for antifungal action and minimum protein concentration for producing a complete inhibition was reported as about 138 mg/mL^[16].

4.8. Anti-fertility activity

The crude extract of bark of *C. papaya* [5–10 mL/(kg-d), *p.o* for 4 weeks] on the seminiferous tubules of rats showed complete loss of fertility attributing to decline in sperm motility and alteration in their morphology. Thus the bark showed the safe and could serve as an effective male contraceptive in animals^[17].

4.9. Histaminergic activity

The crude extract of *C. papaya* (0.5–512 μ g/mL) caused concentration-dependent contraction of ileal strips suspended in tyrode solution which was mediated via H₁-receptor and is dependent on extracellular Ca²⁺ influx^[18].

4.10. Diuretic activity

Aqueous root extract of *C. papaya* when given orally at the dose of 10 mg/kg to rats produced significant increase in urine output and showed similar profiles of urinary electrolyte excretion to that of hydrochlorothiazide^[19].

4.11. Anti-amoebic activity

The study suggested that the cold macerated aqueous

extract of matured papaya seeds (100 μ /mL, *p.o*) showed significant anti-amoebic activity against *Entamoeba histolytica*[20].

4.12. Anti-tumor activity

The aqueous extract of *C. papaya* leaves (0.625–20 mg/mL) exhibits anti-tumor activity. The extract significantly inhibited the proliferative responses of solid tumor cell lines derived from cervical carcinoma (Hela), breast adenocarcinoma (MCF-7), hepatocellular carcinoma (HepG2), lung adenocarcinoma (PCI4), pancreatic epithelial carcinoma (Panc-1) and mesothelioma (H2452) in a dose dependent manner[21].

4.13. Anthelmintic

The dried papaya seeds given as elixir with honey have shown significant effect on the human intestinal parasites, without significant side effects. Benzylisothiocyanate, present in seeds is the chief anthelmintic[22–25].

The latex of papaya has anthelmintic efficacy against *Heligmosomoides polygyrus* in experimentally infected mice, which suggests in potential role as an anthelmintic against potent intestinal nematodes of mammalian hosts[26]. It has also anthelmintic activity against natural infection of *Ascaris suum* in pigs and found to be 100% effective at the dose of 8 g/kg body weight[27].

4.14. Effect on smooth muscles

Ethanol extract of papaya seeds at 0.1–6.4 mg/mL showed concentration dependent inhibition of jejunam contraction and found significantly irreversible. Thus the extract is capable of weakening the contractile capability of isolated rabbit jejunam[28].

4.15. Anti-malarial activity

The petroleum ether extract of the rind of raw papaya fruit at concentration ranging from 0.05–1000 μ g/mL. The extract exhibited significant anti-malarial activity[29].

4.16. Hypoglycemic activity

The ethanolic leaf extract of *C. papaya* at the dose 5.0 mg/kg produced significant blood sugar level reduction with no significant effects at the higher dose of 10 mg/kg. The extract delayed the onset of hypoglycemic activity of glimepiride and increased the hypoglycemic effect of metformin with the variables interacting differently for each drug-extract combinations[30].

4.17. Immuno-modulatory activity

Chemical constituents of the *C. papaya* seed extract and its bioactive fraction were examined *in vitro* using lymphocyte proliferation assays and complement-mediated hemolytic assay[31].

Fermented papaya preparation is a macrophage activator which augments nitric oxide synthesis and tumor necrosis factor- α [32].

4.18. Anti-ulcer activity

Aqueous seed extract of *C. papaya* at the dose of 50 mg/kg and 100 mg/kg *p.o* against alcohol induced acute gastric damage and blood oxidative stress in rats. The gastric acidity was significantly reduced in rats treated with 100 mg/kg of the extract[33].

4.19. Anti-sickling activity

The methanolic extract of *C. papaya* at dose 10 mg/mL *in vitro* reduced hemolysis and protected erythrocyte membrane integrity under osmotic stress conditions[34].

4.20. Administration dependent antioxidant effect

Seeds are the less exploited part thus this study is aimed at assessing the antioxidant activities of the *C. papaya* seeds water extract against hydrogen peroxide (H_2O_2) oxidative stress in human skin Detroit 550 fibroblasts. *C. papaya* seeds water extract is not toxic and acts as a potent free radical scavenger, providing protection to Detroit 550 fibroblasts that underwent H_2O_2 oxidative stress. Data show that (i) the maximum protective effect is achieved by the simultaneous administration of the extract with 1 mmol/L H_2O_2 ; (ii) the extract in presence of an oxidative stress does not increase catalase activity and prevents the release of cytochrome C and the inner mitochondrial transmembrane potential ($\Delta\psi_m$) loss; (iii) the extract is more efficient than vitamin C to hamper the oxidative damage; (iv) the purified subfractions of the seeds water extract exert the same antioxidant effect of whole extract. In conclusion, *C. papaya* seeds water extract is potentially useful for protection against oxidative stress[35].

4.21. Ameliorative effect of leaves of *C. papaya* in hepatotoxicity

The study was performed by administering the aqueous extract of *C. papaya* leaves at the dose of 400 mg/kg in rats prior to administration of ethanol or combination of isoniazid and rifampicin. The effects on the levels of serum indicators of liver damage (ALT, AST, alkaline phosphatase and total bilirubin) and tissue antioxidant parameters like TBARS, GSH and SOD were determined. Histopathology of liver was also performed to study the influence of drug on tissue integrity[36,37].

5. Additional benefits of papaya

Papaya fruit is a rich source of nutrients such as provitamin A carotenoids, vitamin C, B, lycopine, dietary minerals, dietary fibre. Danielone is a phytoalexin found in papaya fruit. This compound showed high antifungal activity against

Colletotrichum gloesporioides, a pathogenic fungus of papaya enzymes to our diet and improved our digestive health. The other benefits of papaya include increase in appetite, relieve nausea, as an acne medicine, ease menstrual pain, lowering the fever, used as a sunscreen and smoothing slave, meat tenderizer and fight from dandruff.

The fruit of papaya can also be used as cosmetics such as improvement of pimples and wrinkles by rubbing the white pulp, good bleaching agent, an important ingredient in bath soap, astringent, hand washes, detergent bars, help in removing dead worn-out skin cells, lightening the colour of our skin.

6. Papaya in case of pregnancy

The main constituents of papaya are papain and chymopapain present in latex showing teratogenic and abortifacient (can induce an abortion) effects. This can cause increase in the chances of uterine contraction as the papain acts like prostaglandin and oxytocin which are known to put a mother's body into labour and hence can cause the adverse effect on babies and mothers health.

The latex can also cause the oedema and haemorrhage placentas, resulting in severe complications in pregnancy and normally an early delivery.

7. Conclusion

The whole plant has its own medicinal value. The various vitamins and enzymes present in the plant (*C. papaya*) make it nutraceutical plant. The papaya has the wide range of pharmacological properties. By the traditional claims papaya is a powerful medicine. Significant amount of work has been done on the biological activities. The present review is about all the pharmacological activities and the uses of chemical constituents.

Conflict of interest statement

We declare that we have no conflict of interest.

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Comments

Background

Detailed study on fruits of *C. papaya* has not been much

carried out. This present review on *C. papaya* was carried out to focus its various pharmacological properties and uses on various disease conditions such as cancer, hypertension, ulcer, malaria *etc.*. The review also focuses its future potential in many diseases on which even the preliminary work has also been not carried out.

Research frontiers

Studies are being performed in order to determine the significant medicinal properties on the basis of traditional claims.

Related reports

Literature survey was done in PubMed using key words *C. papaya*, medicinal properties of *C. papaya*, phytochemicals in *C. papaya*; antioxidants in *C. papaya*, anticancer activity/antidiabetic, activity/anti-inflammatory, activity/wound healing and activity/antifertility effects of *C. papaya*. The articles published only in PubMed indexed journals were primarily considered for writing this review.

Innovations & breakthroughs

The work on fruit of papaya has not been done. So the purpose is to carried out the review on the detailed study of *C. papaya* and its medicinal properties and other additional uses.

Applications

The various applications includes: anti-hypertensive (ethanolic extract of fruit), hepatoprotective (aqueous and ethanolic extract), anti-inflammatory (ethanolic extract), anti-microbial (aqueous extract), anti-cancer, various food industries *etc.*

Peer review

This is a good study in which the evaluation of the various parts of the papaya was carried out by the literature review. The study includes the pharmacological activities, presence of enzymes, traditional uses and nutritional values of the plant.

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