PHARMACY

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SOME ASPECTS OF CARICA PAPAYA LINN AND ITS MEDICINAL USES

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ABSTRACT

Carica papaya L. is grown in plantations and home gardens mostly in the tropical regions of the world. The plants can be classified into three primary sexes, namely, male, hermaphrodite or bisexual and female. Pollination is by wind and insects. Propagation is mainly by seed. Apart from being cultivated for the fruits as a source of food, Carica papaya is also grown for its latex which serves as a rich source of papain used commercially in the cosmetic, textile, food and drug industries. A number of pharmacologically active constituents have been isolated from Carica papaya. Different parts of Carica papaya are used by traditional healers for the treatment of various ailments.

Keywords: Carica papaya, papain, carpaine, benzyl isothiocyanate, anthelmintic

INTRODUCTION

Carica papaya L. popularly known as pawpaw or papaw belongs to the family Caricaceae. Carica papaya is grown extensively throughout the tropical and subtropical regions of the world, both as plantation tree and as favourite fruit for home gardens and farms [10, 13, 32, 54, 60, 66, 75]. The family Caricaceae consists of four genera, namely, Carica, Cyclicomorpha, Jacaratia and Javilla [60, 75]. The genus Carica L. contains about forty species. Papaya is the only species of economic importance in the genus that is cultivated for its edible fruits [60, 66].

Pawpaw is propagated primarily by seed which leads to a great variation between the yields and the quality of individual fruits. Pawpaw can be propagated vegetatively by cutting or grafting, but this is not economical for commercial production. Vegetative propagation is expensive and only used for experimental reasons [31, 60, 63, 66]. A number of varieties of Carica papaya are known: one of the major ones being the 'Solo' variety of Barbados [60, 63, 66, 75]. Other varieties are 'Hortus Gold' of South Africa; 'Improved Petersen' of Australia; 'Betty' of Florida; 'Solo 5', 'Solo 8', 'Solo 10', 'Sunrise', 'Waimanalo', 'Higgis' and 'Wilder' of Hawaii; 'Coorg Honey', 'Co.1', 'Co. 2', 'Pusa 1-15' and 'Banchii' of India; 'Semangka' and 'Thailand' of Indonesia; 'Guinea Gold', 'Sunnybank' and 'Hybrid 5' of Queensland; 'Santa Cruz Giant', 'Cedros' and 'Singapore Pink' of Trinidad; 'Maradol roja', 'Cubana' and 'Paraguanera' of Venezuela; 'Santo 3', 'Santo 4' and 'Santo 7' of Surinam. Other cultivars of merit are 'Bluestem', 'Graham', 'Fairchild' and 'Honey Gold' [1, 7, 27, 49, 50, 61, 63, 66, 71, 75].

In Ghana, apart from the 'Solo' variety, there are hybrids of the cultivars which are referred to simply as the 'Local' variety. This author is not aware of the existence of any documentation of the cultivars available in this country. In this country Carica papaya is found in gardens and farms and often escapes from cultivation. It is widely distributed throughout the country.

Papaya is one of the major export crops of Hawaii; most of the crop is exported in the fresh form [11, 60, 63], while Sri Lanka, Tanzania and Uganda are the primary producers of papain [60, 63, 66]. Papaya is consumed mainly as fresh fruit, but some processed papaya products have been marketed [19, 31, 54, 60, 66]. The major producers of papaya are Brazil, Indonesia, India, Mexico, Hawaii and Zaire [66].

MORPHOLOGY

The stem of Carica papaya is straight, cylindrical, hollow between the nodes except in young plants, usually unbranched but branching may be induced by injury to the apical meristem or by cutting back. It consists mainly of spongy, soft wood parenchyma and bears large, prominent triangular leaf scars, 10-30cm in diameter and 2-10m in height but it is more commonly 4-5m tall. The leaves are clustered near the apex of the trunk and are spirally arranged. They have long hollow petioles 25-100cm long and large deeply-lobed and broadly toothed blades except in the cultivar 'Thailand' of Indonesia which has nearly entire leaves. The leaves are pale green beneath with prominent veins [31, 54, 60, 63, 66, 75].

The plant is dioecious, but hermaphrodite (bisexual) flowers and trees also occur. The female flowers, 3-5cm long, sit alone or in small groups in the leaf axils; the ovary is 2-3cm long and has five fan-shaped stigmas on top. The male flowers, with ten stamens each, are found on long hanging panicles (See Fig.2). Bisexual flowers have either five or ten stamens and some of these tend to become 'carpelloid' (fruit-like) (See Fig.3). Different types of hermaphrodite flowers may occur on the same tree, depending on the season or on the age of the tree [66].

Male trees are also variable. The male tree does not usually produce fruits but sometimes a fruit is found at the end of a long panicle. However, some people believe that by making a cut in the centre of the stem and inserting a stone or by injuring the tree in other ways the male plant can be induced to produce fruit [31, 32]. A complete change of sex may take place when an old male tree is cut back: sprouts bearing female flowers, and later fruits, may appear [66].

Fig. 1 Carica Papaya : Female plant bearing numerous fruits.

Fig. 2 Carica Papaya : Male tree with hanging inflorescences

Fig. 3 Carica Papaya: Stem, leaves and flowers of a hermaphrodite (Bisexual) plant. (Reproduced from Samson, J.A., 1986)

How pollination takes place is not known with certainty; wind is probably the main agent as the pollen is light and abundant, but insects, especially thrips and moths assist [31, 60]. Isolated female trees have set fruit when they were 800 yards from the nearest male tree [60].

The fruit is a large, fleshy, hollow berry. Fruits formed from female flowers are oblong to nearly spherical (See Fig.1), but if formed from bisexual flowers they are pear-shaped, cylindrical or grooved. Fruits weigh from 0.5 to 2kg or more and are 7 to 30cm long. In many countries in Latin America and South Pacific Islands, large size seems to be considered an attribute of desirability and weights of fruits may be from 2.5 to 9.0kg. The thin, green, smooth skin turns yellowish or orange when ripe [16, 51, 60, 66]. The flesh of the ripe fruit is usually yellow to orange in colour but reddish-orange or pink in some cultivars, with the consistency of butter and has a mild and pleasant flavour. The central cavity of the ripe fruit is surrounded by a host of small, spherical, black or greyish, wrinkled seeds enclosed in gelatinous sarcotesta formed from the outer integument [29, 54, 60, 63, 66] but seedless fruits occur too [66].

The root system is extensive and dense or shallow. Actually, a deep and well developed root system may be expected on good soil, whereas the roots will stay near the surface on a wet or compact soil [66].

PROPAGATION

Papaya is normally propagated by seed. Papaya can also be propagated vegetatively by cutting or grafting, but this is not economical for commercial production. Seeds germinate 2-4 weeks after planting if the soil is warm. Papayas thrive on a wide range of soil types in frost-free areas below 1500m in elevation providing that drainage is good. Papayas are tolerant of drought once established but in areas with a pronounced dry season little fruit will be set except during the wet season. Irrigation will increase yields in low rainfall areas but has a disadvantage in that, if irrigation is excessive, the flavour of the fruits may be reduced. Papayas are very responsive to fertilizer and yields can be significantly improved by proper fertilization [54, 60, 63, 66].

Papaya trees begin to bear quickly after planting and will generally produce ripe fruit within a year with the exception of 'Solo' which may take up to 18 months to bear fruit. Yields per tree vary from 30-150 fruits per annum, but 30 fruits per tree per year is considered to be a minimum acceptable yield in many areas. It takes four to six months, depending on climate, for fruits to mature. Although trees may live for 25 years, yields decline with age [54, 60, 63, 66].

MAJOR DISEASES AND PESTS

Few insect pests, e.g. mites, cause serious damage to papayas but damage by disease can be serious and often accounts for the short life of the trees. Seedlings are very susceptible to damping off and older plants are susceptible to root-and collor-rots. All of these fungal diseases are most serious in waterlogged soils. The fungus Glomerella causes anthracnose which causes spotting of ripe fruits and makes the fruit unattractive. Birds damage the fruits too [60, 63, 66]

Mosaic is a very serious disease, caused by a virus transmitted by aphids. The mosaic virus stunts the plants, causes yellow mottling and distortion of the leaves, bending down of petioles followed by death of the tree [60,66]. Perhaps the most potentially serious disease is bunchy top, a mycoplasma disease, caused by a virus transmitted by the leaf hopper, Empoasca papayi [60, 63, 66]. Bunchy top-infected plants yield little or no fruit and should be removed to prevent spread of the virus to healthy plants.

Root-knot nematodes and soil-borne fungi can cause serious replant problems, especially in sandy soils [63, 66].

CHEMICAL COMPOSITION OF CARICA PAPAYA

The water content of the edible portion of fresh papaya fruit is approximately 85 to 88%. Carbohydrate, mainly sucrose, fructose and glucose, vary from 7 to 12%, fat 0.1%, fibre 0.7%, while protein is approximately 0.5%. It contains practically no starch. Papaya is a rich source of vitamin A and has fair amounts of vitamins B_1, B_2 and C. 100g of the flesh contains carotene (2500 i.u.), ascorbic acid (30-120mg), calcium (20mg), iron (0.5mg) and thiamine (0.03mg) [12, 51, 54, 60, 66]

The volatile components of Carica papaya fruits have been analysed by Katague and Kirch [34]. In their study, homologous series of normal primary alcohols from C_1 to C_6 and primary isoalcohols from C_3 to C_5 were found along with the corresponding acetate esters. Ethyl, propyl, butyl and hexyl alcohols and methyl, ethyl, amyl and isoamyl acetates were found to be present in relatively high concentrations (greater than 5%). Amyl and isoamyl alcohols and heptanone-2 were found to be present in quantities less than 1%. Also found were isopropyl alcohol, propyl acetate and butyl acetate. The concentrations of these components varied at different stages of ripening. As the fruit ripens a decrease in the concentrations of methyl alcohol, methyl acetate, ethyl acetate, and hexyl alcohol and a marked increase in the concentrations of ethanol and isoamyl acetate were noted. In another study, Flath and Forrey [23] examined the concentrated volatile components of the fresh Carica papaya fruits and a total of 106 components, mainly alcohols, aldehydes and esters, were identified. Linalol was the major component of the concentrates followed by benzyl isothiocyanate.

The nonvolatile acids of papaya of the common commercial variety ('Solo') were examined by Chan, Jr., Chang, Stafford and Brekke [10]. In this study the nonvolatile acids were extracted from papaya puree, separated by thin-layer chromatography and identified as α-ketoglutaric, citric, malic, tartaric, ascorbic and galacturonic acids. Quantitative determination by gas-liquid chromatography showed malic and citric acids to be present in approximately equal amounts, 0.464 and 0.525 mequiv per 100g wet weight, respectively. They were about ten times more abundant than α-ketoglutaric acid, of which there was only 0.042 mequiv per 100g.

The total titratable acidity of papaya was 1.54 mequiv per 100g. Papaya puree had 0.279 mequiv of ascorbic acid per 100g (49.2mg per 100g) which, together with the malic, citric and α- keto glutaric acids, totaled 1.31 mequiv per 100g, about 85% of the total titratable acidity. Total volatile acids in papaya were 0.123 mequiv per 100g and contributed 8% to the total titratable acidity. The remaining 7% (0.11 mequiv per 100g) was attributed to galacturonic, tartaric, pectic and unidentified nonvolatile acids [10].

Chan, Jr., and Kwok [12] have provided positive evidence for the presence in papaya of high concentration of invertase, an enzyme which converts sucrose to glucose and fructose in papaya puree. Papaya puree prepared by macerating papaya fruit without special treatment invariably develops off-flavours and off-odours due to enzymatic or microbial activity. The development of undesirable odours was investigated in papaya purees prepared in laboratory and pilot plant operations. Butyric, hexanoic and octanoic acids and their methyl esters were found in purees prepared by commercial methods; these samples had strong off-odours and off-flavours. In an improved method of processing papaya puree, acidification and heat inactivation of enzymes prevented development of the compounds which contributed to unpleasant odours and flavours [11].

The chemical composition of <u>Carica papaya</u> seeds has been determined by Marfo, Oke and Afolabi [43]. According to these authors, the seed is a rich source of proteins, lipids and crude fibre. These authors demonstrated the presence of glucosinolates, tannins and phytates in papaya seed and suggested that the occurrence of these toxicants in the seed may limit the use of the papaya seed and its oil for animal or human consumption. Feeding trials in rats have actually confirmed the unsuitability of papaya seed oil for human consumption. Prolonged use of papaya seed oil may lead to fatty liver and kidney and probably heart disease [44]. Fatty acids present in measurable quantities in papaya seed oil are oleic acid, palmitic acid, linoleic acid, stearic acid, myristic acid and lauric acid [43]. Sucrose is the predominant saccharide in the seed but the monosaccharides, glucose, fructose and galactose also occur in the seed. Calcium and phosphorus levels are high in papaya seed [43]. Dar, Garg and Pathak [17] have reported carpasemine and benzyl isothiocyanate as being the major components of the papaya seed.

<u>Carica papaya</u> is grown also for its latex which contains four components with proteolytic activity, three of which have been identified as papain, chymopapain and peptidase A. They represent 5, 27 and 14% of the latex protein respectively. All parts of the plant contain this latex which can be seen exuding freely as a white sap when the plant is wounded. However, the greatest amount of the latex is in the mesocarp of the unripe fruits [32, 60., 63, 65, 66, 67, 75].

A number of alkaloids have been isolated from <u>Carica papaya</u>. These include carpaine which occurs in all the green parts of the plant [5, 9, 24, 26, 28, 32, 55] and pseudocarpaine [24, 25]. Smalberg, Rall and De Wall [70] isolated four alkaloids, nicotine, conitine, myosmine and a fourth alkaloid that was not identified from alcoholic extract of <u>Carica papaya</u> leaves.

USES OF <u>CARICA PAPAYA</u>

The ripe fresh fruit is eaten throughout the tropics for breakfast. It is also used for fruit salads and desserts. Recently, papaya is being sold regularly on markets of temperate countries. It is used for making soft drinks, jam, ice-cream, flavouring, crystallized fruit and is canned in syrup. Processed papaya fruit has a neutral taste that is greatly improved by the addition of passion fruit juice. Unripe fruits are cooked as a substitute for marrow and for apple sauce. Young leaves are sometimes eaten as spinach. In Java a sweetmeat is made from the flowers. The flowers and the stem, after removal of the bark, are eaten in Malaya. The leaves and young fruits are used to tenderize meat. Older leaves are sometimes dried and used like tobacco for smoking [29, 31, 32, 51, 54, 60, 66]. The fruit pulp of <u>Carica papaya</u> is used for thickening of pharmaceuticals, cosmetics and dentifrices [41].

PHARMACOLOGICAL CONSIDERATIONS AND MEDICINAL USES OF CARICA PAPAYA

Aeroallergens of Carica papaya e.g. pollen, cause bronchial asthma and may cause other allergic reactions following accidental contact with the flowers, or if the sensitized individual is adjacent to the plant [37]. Carica papaya is included in a compilation of plants claimed to show experimental hypoglycaemic activity [38].

The pharmacological properties of carpaine have been well documented. The Japanese have reported it to be effective in the treatment of amoebic dysentery [77]. The latex of papaya is employed as an amoebicide in Central America [40] probably due to its carpaine content. Ramsewamy and Sirsi [62] found carpaine to inhibit Mycobacterium tuberculosis at a low dilution.

Carpaine produced a dose-dependent effect in lowering the blood pressure and heart rate of the rat [30] and the cat [78]. The hypotensive and bradycardial effects of carpaine were not mediated through the autonomic nervous systems since selective autonomic blockade with atropine and propranolol did not alter the circulatory responses to carpaine [30]. These findings contradict the earlier suggestions that carpaine may have pharmacological properties similar to those of digitalis [22, 52, 54].

Tuffley and Williams [78] and Hornick, Sanders and Lin [30] have reported that carpaine affects the myocardium directly. Hornick and co-workers [30] suggested that the observed effects of carpaine on the myocardium may be related to its macrocyclic dilactone structure, a possible chelating structure. If the free calcium ions in the plasma were taken up by carpaine a lowered cardiac performance would result.

Employing in vitro preparations, Tuffley and Williams [78] found that carpaine produced a relaxation of guinea-pig uterus, dilatation of guinea-pig bronchioles, but the frog was relatively insensitive to the drug. Carpaine was also found to be effective as an anti-tumour agent [56]. The latex too is used externally for treating malignant tumours [32].

Papain, chymopapain and peptidase A are found in the latex obtained from all parts of the Carica papaya plant. Papain is the most studied, though the crude papain is a mixture of all three enzymes. Papain, a proteolytic enzyme, is used in meat tenderizing, manufacture of chewing gum, in cosmetics, in the tanning industry for bating hides, in textile manufacture for degumming natural silk and to give shrink-resistance to wool, and in brewing for making 'chill-proof' beer. Papain acts in acid, alkaline and neutral media and is used in medicine to strengthen digestion beyond as well as in the stomach [4, 29, 32, 51, 54, 60, 63, 66]. Papain is used for the treatment of insect stings [3], jelly fish stings [42] and for debridement of burn eschars and necrotic tissue [68]. Papain has analgesic and anti-inflammatory activities [21]. The drug has been used in both animals and humans to remove cataract [15, 73, 74].

Some unwanted effects of papain have been reported. Papain has induced asthma in meat tenderizing workers who have had to be exposed to papain dust. Immunological studies in these patients have revealed the presence of specific IgE and IgG antibodies [53, 76]. Reports of the pathology of papain in man appear to be limited to allergic reactions of asthma, rhinitis, urticaria, angioedema and anaphylaxis [8, 46, 57].

Papain has been shown to produce teratogenic and embryotoxic effects in pregnant rats and rabbits [69]. Papain causes degeneration of rat placentae [18] and dissolves the chorion [33].

The unripe fruits and seeds of Carica papaya have been used in some parts of India for criminal abortion [47] and because of this pregnant women in these parts of India are strictly prohibited from eating Carica papaya fruits at any time during pregnancy for fear of inducing abortion [80]. The abortifacient properties of papaya are known in many other countries too including Ghana. The roots, ground with salt and mixed with water and used as enema, are abortifacient in Ghana [32]. The seeds are believed to cause abortion. A leaf decoction used as purgative and an infusion of the dried leaves drunk for stomach complaints may even cause abortion. The young fruits when boiled form a useful vegetable, though thought to cause abortion [32, 58, 59].

The seed of Carica papaya has anthelmintic property [2, 32, 36, 45, 48, 58, 59, 60, 64, 66]. The major components of the seed are carpasemine and benzyl isothiocyanate and the anthelmintic property has been attributed principally to benzyl isothiocyanate [17].

The anthelmintic action of the extract from Carica papaya seed was believed to be due to its ability to block neuromuscular activity of the ascaris worms [2, 8, 35, 64]. However, El-Tayeb, Kucera, Marquis and Kucerova [20] have reported that the lack of effect of benzyl isothiocyanate on the rat phrenic nerve hemi-diaphragm preparation does not support the mechanism of action of most anthelmintics that block neuromuscular junction of ascaris worms, and therefore it may not effect its action through the

Recently, Paninga [58] and Wambebe,

Abaitey and Paninga [79] have reported that the extract from Carica papaya seed affects isolated skeletal muscle preparations (including the rat phrenic nerve hemidiaphragm preparation) directly resulting in permanent contracture, suggesting that the extract could be acting at a point beyond the neuromuscular junction. These authors have proposed that the extract is likely to be interfering with the process involved in either sequesteration of released calcium ions or the storage of calcium ions thereby making calcium ions continuously available for the sustained and irreversible contracture.

Different parts of Carica papaya have been used for various purposes. The roots of the male plant are used to cause immediate delivery [72], for stomachache [59] and for treating yaws, piles and headache [32]. An infusion from the young leaves is used for gonorrhoea, and the crushed leaves are said to be styptic and to heal wounds. The leaves and roots are used as anthelmintic and a leaf decoction is used as purgative [32,59]. The inner bark of papaya is used in Samoa for sore teeth [39]. In Nigeria the latex from unripe fruits is said to be a vermifuge. It is claimed that the latex from crushed fruits is massaged on the breast or the breasts exposed to boiling fruits to induce the flow of milk (sympathetic magic?) [32].

CONCLUSION

Traditional healers worldwide have claimed success in the treatment of several diseases such as breast cancer, malaria, sickle cell anaemia, veneral diseases, hypertension, diabetes, mental diseases and recently aids. As a result of these claims, developing herbal medicine has become a topic for discussion in various West African countries including Ghana. There are good economic and social reasons in favour of the development of herbal medicine in Ghana. It can be cheap, locally available and culturally acceptable to the majority of our people.

Many plants that have proved efficacious in folklore herbal medicine have been shown scientifically to contain compounds that justify the use of these plants in traditional medicine. Ghana abounds in many medicinal flora like carica papaya with proven therapeutic and commercial potentialities. Scientific investigations of such medicinal plants and their incorporation into our health care delivery system will help cut down the national drug bill considerably.

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