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Carica Papaya- A Herbal Medicine

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Abstract: *Medicinal plants have played an essential role in the development of human culture. Carica papaya Linn.is a monoecious, dioecious or hermaphrodite tree; it belongs to the family Caricaceae. It is widely cultivated throughout world and is used as food and traditional medicine, particularly as an antiseptic and contraceptive. Papaya contains many biologically active compounds. Fruit, leaves, latex and stem are used to treat indigestion, diarrhoea, swelling of the lungs, stoppage of urination, blindness, tachycardia, ringworm and alopecia. The papaya is a nutritive fruit containing a small amount of proteins and the same amount of minerals consisting mainly of iron, calcium and phosphorus, vitamin A and C and is rich in the enzyme papain. The seeds of Papaya have been reported to have both antimicrobial and antihelmintic activities. The latex of Papaya and fluconazole has synergistic action on the inhibition of the growth of Candida albicans. The molluscicidal activity of C. papaya seed and latex may be due to the presence of papain.*

Keywords: *Carica papaya, Alkaloids, Antioxidants, Antehelminthes, Herbs*

1. INTRODUCTION

Medicinal plant is an important element of indigenous medical systems in all over the world. The ethno botany provides a rich resource for natural drug research and development (Farnsworth, 1990). Natural products have played an important role throughout the world in treating and preventing human diseases. *Carica papaya Linnaeus*, (pawpaw), belongs to the family of Caricaceae (Jaiswal, et al., 2010). It is herbaceous succulent plant with self-supporting stems. **(**Mello, et al., 2008). Bamisaye, et al., (2013) reported that it is a large tree-like plant with a single stem growing from 5 to 10 meters tall with sparely arranged leaves confined to the top of the trunk. The lower trunk is conspicuously scarred where leaves and fruits were borne (Bamisaye, et al., 2013). He also reported that all parts contain latex. It generally branches only when injured (Mello, et al., 2008). Originally derived from the southern part of Mexico, *Carica papaya* is a perennial plant (Bruce and Peter, 2008). The hollow green or deep purple trunk is straight and cylindrical with prominent leaf scars. Its diameter may be from 2 or 3 inches to over a foot at the base. Mali and Mehta, (2008) reported that fruit, leaves, latex and stem are used to treat indigestion, diarrhoea, swelling of the lungs, stoppage of urination, blindness, tachycardia, ringworm and alopecia. Saleh, (2015) experimented that products of higher plant origin have been known to be effective sources of chemotherapeutic agents without any underlying effects and they are the major source of medicines, as they have been throughout human history. Akinyemi et al. (2006) reported that the use of medicinal plants all over the world predates the introduction of antibiotics and other modern drugs. A medicinal plant is any plant with one or more of its organs containing substances that can be used for therapeutic purposes or which are the precursors for the synthesis of useful drugs (Jahan, et al., 2011). They are of great importance to the health of individuals and communities; the medicinal values of certain plants lie in some chemical substances that produce definite physiological action on the human body (Akinyemi, et al., 2006, Jahan, et al., 2011). Bamisaye, et al. (2013) noted that the most important of these bioactive constituents of plants are lavonoids, tannins, alkaloids and foods plants sometimes added to foods. These active principles or ingredients occur naturally in such plants (Bamisaye, et al., 2013). Amongst such medicinal plants is Pawpaw *(Carica papaya)*. Herbal medicine is gaining popularity in developing countries (Rahman, et al., 2013). Herbal treatments involve mainly the use of plant extracts and other plant products (Rahman, et al., 2013) which contain bioactive substances. These phytochemicals have potentials to prevent or cause adverse effects (Unnikrishnan, 2008). For

example, alkaloids are used medicinally as analgesics or anaesthetics and are also used as antimalarial, antihypertension and local anaesthesia in ophthalmology. Alkaloids are also central nervous system stimulants (Srivastava and Singh, 2015). Woolley**, (**2001) reported that they have anthelmintic properties and serve as aphrodisiacs in the treatment of erectile dysfunction. Our study identified that alkaloid is one of the major constituents in *Carica papaya* and form the basis for its being use in the management of erectile related dysfunction and several other disorders (Woolley, 2001). The World Health Organization (WHO) has also recognized the importance of traditional medicine and has created strategies, guidelines and standards for botanical medicines. Proven agro-industrial technologies need to be applied to the cultivation and processing of medicinal plants and the manufacture of herbal medicines (WHO,1993). Medicinal plants are resources of new drugs and many of the modern medicines are produced indirectly from plants. It is estimated that there are more than 250,000 flower plant species. Studying medicinal plants helps to understand plant toxicity and protect human and animals from natural poisons. In this review the objective is to consider the value of medicinal plants such as *C. papaya* used in traditional and modern medical practices as bioactive natural compounds.

2. CHEMICAL COMPOSITION

Phytochemical analysis of the *C. papaya* showed the presence of saponins, alkaloids, tannins, flavonoids, cardiac glycosides, anthraquinones, phlobatinins, anthocyanosides and phenols (Imaga, et al., 2010). The presence and compositions of these various phytochemicals vary from one plant part to the other and is determined by the solvent used for extraction (Doughari, et al., 2009, Imaga et al., 2010). Kumar, et al. (2013) reported that the papaya is a nutritive fruit containing a small amount of proteins and the same amount of minerals consisting mainly of iron, calcium and phosphorus, vitamin A and C and is rich in the enzyme papain.

3. ACTIVE COMPONENT AND THEIR ACTION

Papaya contains many biologically important active compounds such as chymopapain, papain, caricain, and glycyl endopeptidase and papaya lipase. (Yogiraj, et al., 2014, Aravind, et al., 2013, Chaiwut, et al., 2007). Chaiwut, et al. (2007) reported that papaya latex proteases are composed of cysteine proteases which contribute 69- 89% of total protein: less than 10% papain, 26-30% chymopapain, 23-28% glycyl endopeptidase, and 14-26% caricain. These four proteases have similar molecular weight of approximately 23 kDa. Poulter & Caygill (1985) reported that their proteolytic activities are activated by additions of small reducing agent such as cysteine and a chelating agent like EDTA. It has been shown that proteases from latex of the fruit differ from those of the non-fruit parts (Brocklehurst and Salih, 1985, Mckee and Smith , 1986) and even from latex of newly wounded fruits (Azarkan, et al., 2004, 2006). The major component in the non-fruit enzymes is chymopapain and the proportions of other enzymes are greatly reduced from the latex proteases (Brocklehurst and Salih). A series of low molecular weight proteins are found in the latex obtained from newly wounded fruits (Azarkan, et al., 2004). Whereas, repeatedly wounded fruits accumulate and/ or activate several enzymes including papain, chymopapain and caricain (Azarkan, et al., 2006). Proteases in *Carica papaya* are cysteine proteases which need small reducing agents such as cysteine to activate them before catalysis of the reaction. These reducing agents convert reversibly inactive forms of enzymes to the active forms and protect their catalyzed essential thiol group from oxidation (Poulter and Caygill, 1985, Caygill, 1979).

4. MEDICINAL PROPERTIES

The various parts of the *Papaya* plant have been reported to possess medicinal properties in the treatment of various ailments and human diseases (Okeniyi, et al., 2007, Owoyele, et al., 2008, Adigwe, et al., 2012). The aqueous seed extract of the unripe mature fruit of *Carica papaya* has been shown to have nephron protective activity (Adeneye, et al., 2009, Olagunju, et al., 2009). The *Papaya* fruits are used as topical ulcer dressings in Jamaica (Hewitt, et al., 2002, Adigwe, et al., 2012). Okeniyi, et al. (2007) reported that seeds of *Papaya* have both antimicrobial and antihelmintic activities. The latex of *Papaya* and fluconazole has synergistic action on the inhibition of the growth of *Candida albicans* (Giordani, et al., 1997, Roshan, et al., 2014). *Carica papaya* plants produce natural compounds in leaf bark and twig tissues that possess both highly anti-tumour and pesticidal properties (Jaiswal, et al., 2010. It was suggested that a potentially lucrative industry based simply on production of plant biomass could develop for production of anti-cancer drugs, pending Food and

Drug Agency approval, and natural pesticides (Roshan, et al., 2014). Kalou, et al. (2011) concluded that self-defence compounds in the tree makes it highly resistant to insect and disease infestation. *Carica papaya L*. leaf tea or extract has a reputation as a tumour-destroying agent. (Kalou, et al., 2011). The seed is used for intestinal worms when chewed (Ayoola and Adeyeye, 2010). The root is chewed and the juice swallowed for cough, bronchitis, and other respiratory diseases. Ayoola and Adeyeye, (2010) reported that unripe fruit is used as a remedy for ulcer and impotence. Fresh, green pawpaw leaf is an antiseptic, while the brown, dried pawpaw leaf is the best as a tonic and blood purifier. It cleans the intestines from bacteria, more so that (only a healthy intestine is able to absorb vitamin and minerals, especially vitamin B12) (Dev and Iqbal, 2015).Chewing the seeds of ripe pawpaw fruit also helps to clear nasal congestion, (Elizabeth, 1994, Eleazu, et al., 2012). The green unripe pawpaw has a therapeutic value due to its antiseptic quality. The tea, prepared with the green papaya leaf, promotes digestion and aids the in treatment of ailments such as chronic indigestion, overweight and obesity, arteriosclerosis, high blood pressure and weakening of the heart (Saran and Chaudhary, 2013).

5. ANTHELMINTIC PROPERTIES

Helminthiasis is a disease in which a part of the body is infested with worms such as pinworm, roundworm or tape worm. Raju and Yesuf, (2010) observed that the worms reside in the gastrointestinal tract and also burrow into the liver and other organs. They produce harmful effect on host by depriving him of food, causing blood loss and by secreting toxins. Dwivedi, et al. (2011) noted that anthelmintic are drugs that act locally to expel parasitic worm from gastrointestinal tract. Papaya seeds are used as anthelmintics. Recent years, papaya latex and its commercial products have been widely applied in baking and beverage industries, pharmacy and new chemicals synthesis (Ortega, 2011). Kanthal, (2012) reported the antehelminthic properties of papaya on adult Indian earthworm, *Pheretima posthuma* due to its anatomical and physiological resemblance with the intestinal roundworm parasite of human beings. Because of easy availability, earthworms have been used widely for the initial evaluation of anthelmintic compounds in vitro.

6. ANTIFUNGAL ACTIVITY

Kumar et al 2013 reported that Antifungal activity of the *Carica papaya* plant against the pathogenic fungi viz. *Aspergillus niger, A. flavus, Candida albicans* and *Microsporum fulvum* . and observed 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. Moulds and yeasts are so widely distributed in human environment that human beings are instantly exposed to them. Fortunately, because of the relative resistance of human beings and comparatively non pathogenic nature of fungi, most of these exposures do not lead to over infection (Kumar, et al., 2013). However, fungi are gaining importance with respect to increased incidence of chronic, often fatal, mycoses in immune compromised patients (Blanco and Garcia, 2008). The fungi present in soil, water and air constitute exogenous fungal opportunists. The roster of opportunistic fungal species continues to increase. However, some of the common ones include *Aspergillus fumigates A.niger A.terreus ,A. flavus, Absida, Candida albicans,Cryptococous neoformis, Microsporum fulvum, Mucor, Rhizomucor, Rhizopus and Torulopsis globrata* (Kumar et al 2013). To find suitable drug for the management of fungal diseases is difficult because fungi, like human beings, are eukaryotes. Giordani, et al. (1997) reported the antifungal activity of *C. 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. Roshan, et al. (2014) noted that a mixture of *C. papaya* latex (0.41 mg protein/ml) and fluconazole (2 µg/ml) also showed a synergistic action on the inhibition of *C. albicans* growth.

7. MOLLUSCICIDAL ACTIVITY

A large number of snails though harmless in their eating habits are intermediate hosts of helminth parasites and are thus responsible for the spread of serious parasitic infections (Singh, et al., 2012). Two important diseases spread by snails are fasciolosis and schistosomiasis caused by *Fasciola hepatica* and *Schistosoma*, respectively (Singh, et al., 2012). The life cycle includes fresh water snails *Lymnaea acuminata* (Lymnaeidae) and *Indoplanorbis exustus* (Planorbidae) as an intermediate host of the parasite ((Agarwal and Singh, 1988, Srivastava and Singh, 2015). Srivastava and Singh, 2015

reported that feeding of snail attractant pellets containing papain (40% of 24 h LC50) caused significant reduction in the level of protein, amino acids, DNA, RNA and AChE activity in the gonadal/nervous tissue of *Lymnaea acuminata. Carica. papaya* seed and latex are potential source of botanical molluscicides. *C. 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 (Srivastava, 2013). Papain occurs in all parts of the tree except the root (Islam, et al., 2014). Jaiswal, et al., (2010) reported that 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 *C. 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.

8. ANTIOXIDANT ACTIVITY

The major groups of phytochemicals that have been suggested as a natural source of antioxidants may contribute to the total antioxidant activity of plant materials including polyphenols, carotenoid and traditional antioxidant vitamins such as vitamin C and E (Maisarah, et al., 2013). Antioxidant is any substance that when present at low concentration compared to those of an oxidisable substrate significantly delays or prevents oxidation of that substrate (Maisarah, et al., 2013). Antioxidant functions are associated with decreased DNA damage, diminished lipid per oxidation, maintained immune function and inhibited malignant transformation of cells (Gropper, et al., 2009, Swathi, et al., 2016). Several studies showed that phenolic compounds are the major bioactive phytochemicals with human health benefits (Swathi, et al., 2016). Mehdipour, et al. (2006) 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 (Jaiswal, et al., 2010). 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 (Jaiswal, et al., 2010). 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 (Mehdipour, et al., (2006). 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 anti- oxidative stress potential of *C. papaya* juice, which was found to be comparable to the standard antioxidant compound alpha tocopherol (Jaiswal, et al., 2010). Nakamura (2007) reported that hexane extract of *C. papaya* seed homogenate is highly effective in inhibitory superoxide generation and apoptosis in H2-60 cells. Olagunju (2009) observed that the aqueous seed extract of the unripe mature fruits of *Carica papaya* has nephro protective. It is due to its antioxidant or oxidative free radical scavenging activities (Jaiswal, et al., 2010).

9. ANTI-REPRODUCTIVE ACTIVITY

Srivastava, (2013) reported that feeding of bait formulation of papain with attractant (starch or serine) have sufficient molluscicidal activity against *L. acuminata.* Sub-lethal (40% and 80% of 24h LC_{50}) of feeding of bait containing plant molluscicides papain significantly reduced the fecundity of the snail *L. acuminata*. The CDC cells (caudo dorsal cells) in the brain of the snail *L. acuminata* release ovulation hormone (Roubos, et al., 1981). The cerebral neurosecretory caudo dorsal cells (CDC_S) of the fresh water pulmonates snail *Lymnaea stagnalis* control egg laying, an event that involves a pattern of stereotyped behaviour (Vreugdenhil, 1988). The CDC_S synthesize and release multiple peptides, among which is the ovulation hormone (CDCH). It is thought that each peptide controls a specific aspect of the processes involved in egg laying (Vreugdenhil, 1988). It seems that after sublethal treatment of papain caused the decrease the level of serotonin and inhibits prostaglandins synthesis by inhibiting 5-lipoxygenase and leukotriene directly or indirectly CDCs. Possibly, the active molluscicidal component papain affect the CDCs and reduce the release of ovulation hormone, resulting a decrease in the fecundity of treated snail.

10. CONCLUSION

Papaya plant is mainly used as the food ingredient throughout the world because of its fruits and its nutritive values. From the above studies about the papaya plant shows that the plant's leaves, stem, fruits and seeds also contains different chemical constituents such as Alkaloids carpain,

pseudocarpain, dehydrocarpaine I and II, choline, carposide, vitamin C and E. Carposide and an enzyme myrosin, sinigrin, Carpaine, benzylisothiocyanate, benzyl glucosinolate, glucotropacolin, benzylthiourea, hentriacontane, β-sitosterol, caricin, leaves related alkaloids, flavonoids, saponins, tannins, cardiac glycoside, anthraquinones and cardinolodes etc. many of the pharmacological activities has been done on the papaya plants. But hence extensive investigations on its pharmacodynamics, kinetics, proper standardization and clinical trials are needed to exploit their therapeutics utility to cure many diseases.

AUTHORS' CONTRIBUTION

Both authors contributed equally to this work, read and approved the final manuscript.

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