

Health Benefits, Chemistry and Mechanism of Carica Papaya a Crowning Glory

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Abstract

Mini review article highlights about the health benefits, chemistry and mechanism of papaya. Fruit and vegetables cannot be equated to that promised by nutritional pills and supplements. Nutrition experts advocate generous intake of fruits for optimum health as these food items are loaded with all the benefits. Especially papaya fruits is goldmine of vitamins C, E, K, minerals and fiber and ideal to consume at least 4-5 servings in a day. Since they are in natural form, account for largest part of water and 100% bad cholesterol free, it's much easier for the body to process and absorb the vitamins and minerals from the fresh fruit. The chemical action of acyltransferase is studied which is extracted from ripened papaya fruit and then benzyl alcohol is acylated to give benzylacetate.

Key words: Papaya; Health benefits; Mmechanism; Vitamins; Gold mine

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1. INTRODUCTION

1.1 History & Description of Papaya

The first literary reference to papayas dates back to 1526, when they were found in the Caribbean coast of Panama and Colombia and described by the Spanish chronicler Oviedo Hankinson S E (Attar et al., 2004). Though it resembles a tree, a papaya plant is actually an overgrown

herb, known as an herbaceous perennial. Eventually, it grows to 20 to 30 feet, producing melon-like oval fruits six to 20 inches long Ensminger A H (Auria, Chen, & Pichersky, 2002).



Figure 1
Carcifera Papaya Ensminger A H

Thanks to its several hardy seeds (which can last for up to the 3 years in cool and dry conditions) the plant spread relatively easily throughout the tropics, and has become naturalized in several regions, especially those abundant with water and fertile soils. It is believed papaya is a native to tropical America, in a region that goes from the Andes of South America to Southern Mexico. It was taken by the Spaniards to Manila in the mid-16th century and gradually spread to all tropical and subtropical countries. It is now widely cultivated in India, China, Sri Lanka, Malaya, Mexico, Brazil, Peru, Venezuela, Central and South Africa,

Philippines, Australia and on most of the Pacific islands Hankinson S E & Ensminger A H (Attar et al., 2004; Auria, Chen, & Pichersky, 2002). In Florida, during the early 1900, there was a small papaya industry, but it was rapidly destroyed by viral diseases (such as papaya ring spot virus) that are still threatening papayas in other areas: the Hawaii and industry underwent a decline recently for this reason.

“Papaya” is recommended to be one such pick from the group of Yellow and orange fruits, which promises abundant health benefits. It is a melon like fruit with yellow- orange flesh with dozens of small black seeds enclosed in skin that ranges in color from green to orange Hankinson S E (Attar et al., 2004). It is a large, fleshy, hollow berry up to 50-60 cm. in diameter and usually weighs from 1/2 kg. to 2 kg. It is cylindrical or pear-shaped. The central cavity is surrounded by hundreds of small seeds, though sometimes seedless varieties of the fruit are also found.

The fruit has a thin smooth skin. It is dark green in color at first, but as the papaya ripens, it changes to bright yellowish or orange. Inside, the thick juicy flesh has a soft melting quality, and may be yellow or pink. It has a delicate aroma and delicious flavor.

The fruit, as well as the other parts of the papaya tree, contain papain, an enzyme that helps digest proteins. This

enzyme is especially concentrated in the fruit when it is unripe. Papain is extracted to make digestive enzyme dietary supplements and is also used as an ingredient in some chewing gums Ensminger A H (Auria, Chen, & Pichersky, 2002).

1.2 Papaya is Rich in Nutrient Content

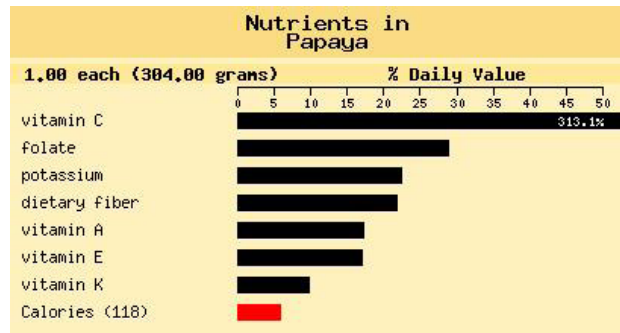


Figure 2
Papaya Has High Nutritional Benefits Ensminger A H

The above is a chart which graphically details the % DV that a serving of papaya provides for each of the nutrients. Nutrients value of papaya per 100 gms is also discussed later on McKinstry LA (Baybutt, Hu, & Molteni, 2000).

Table 1
Nutritive Value of Papaya per 100 gm McKinstry LA.

Nutrient	Units	Value per 100 grams	Number of data points	Std. error
Proximates				
Water	g	88.83	36	0.3
Energy	kcal	39	0	0
Energy	kJ	163	0	0
Protein	g	0.61	31	0.031
Total lipid (fat)	g	0.14	10	0.042
Ash	g	0.61	33	0.03
Carbohydrate, by difference	g	9.81	0	0
Fiber, total dietary	g	1.8	0	0
Sugars, total	g	5.90	0	0
Minerals				
Calcium, Ca	mg	24	5	7.198
Iron, Fe	mg	0.10	20	0.019
Magnesium, Mg	mg	10	20	1.825
Phosphorus, P	mg	5	20	0.481
Potassium, K	mg	257	14	27.569
Sodium, Na	mg	3	14	0.355
Zinc, Zn	mg	0.07	2	0
Copper, Cu	mg	0.016	18	0.001
Manganese, Mn	mg	0.011	18	0.001
Selenium, Se	mcg	0.6	0	0

Table 2
Nutrients and Minerals of Papaya

Nutrient	Units	Value per 100 grams	Number of data points	Std. error
Vitamins				
Vitamin C, total ascorbic acid	mg	61.8	89	2.244
Thiamin	mg	0.027	17	0.002
Riboflavin	mg	0.032	19	0.002
Niacin	mg	0.338	15	0.036
Pantothenic acid	mg	0.218	0	0
Vitamin B-6	mg	0.019	1	0
Folate, total	mcg	38	0	0
Folic acid	mcg	0	0	0
Folate, food	mcg	38	0	0
Folate, DFE	mcg_DFE	38	0	0
Choline, total	mg	6.1	0	0
Vitamin B-12	mcg	0.00	0	0
Vitamin B-12, added	mcg	0.00	0	0
Vitamin A, RAE	mcg_RAE	55	0	0
Retinol	mcg	0	0	0
Carotene, beta	mcg	276	6	214.25
Carotene, alpha	mcg	0	3	0
Cryptoxanthin, beta	mcg	761	6	243.775
Vitamin A, IU	IU	1094	0	0
Lycopene (1)	mcg	0	3	0
Lutein + zeaxanthin	mcg	75	3	0
Vitamin E (alpha-tocopherol)	mg	0.73	0	0
Vitamin E, added	mg	0.00	0	0
Vitamin K (phylloquinone)	mcg	2.6	0	0
Lipids				
Fatty acids, total saturated	g	0.043	0	0
4:0	g	0.000	0	0
6:0	g	0.000	0	0
8:0	g	0.000	0	0
10:0	g	0.000	0	0
12:0	g	0.001	2	0
14:0	g	0.007	3	0
16:0	g	0.032	3	0
18:0	g	0.002	3	0
Fatty acids, total monounsaturated	g	0.038	0	0
16:1 undifferentiated	g	0.020	3	0
18:1 undifferentiated	g	0.018	3	0
20:1	g	0.000	0	0

To be continued

Continued

Nutrient	Units	Value per 100 grams	Number of data points	Std. error
22:1 undifferentiated	g	0.000	0	0
Fatty acids, total polyunsaturated	g	0.031	0	0
18:2 undifferentiated	g	0.006	3	0
18:3 undifferentiated	g	0.025	3	0
18:4	g	0.000	0	0
20:4 undifferentiated	g	0.000	0	0
20:5 n-3	g	0.000	0	0
22:5 n-3	g	0.000	0	0
22:6 n-3	g	0.000	0	0
Cholesterol	mg	0	0	0
Amino acids				
Tryptophan	g	0.008	6	0
Threonine	g	0.011	1	0
Isoleucine	g	0.008	1	0
Leucine	g	0.016	1	0
Lysine	g	0.025	7	0
Methionine	g	0.002	5	0
Phenylalanine	g	0.009	1	0
Tyrosine	g	0.005	1	0
Valine	g	0.010	1	0
Arginine	g	0.010	1	0
Histidine	g	0.005	1	0
Alanine	g	0.014	1	0
Aspartic acid	g	0.049	1	0
Glutamic acid	g	0.033	1	0
Glycine	g	0.018	1	0
Proline	g	0.010	1	0
Serine	g	0.015	1	0
Other				
Alcohol, ethyl	g	0.0	0	0
Caffeine	mg	0	0	0
Theobromine	mg	0	0	0

1.3 Papaya Facts and Trivia

Papaya trees can grow from a seed to a fruit bearing tree in less than 18 months.

Due to its high content in a proteolytic enzyme called “papain”, papaya extracts are sold in a white powder, with added salt, sugar and anticaking agents, as a meat tenderizer. South American aborigens used papaya juice as a meat tenderizer for centuries McKinstry LA (Baybutt, Hu, & Molteni, 2000).

There are two most common varieties of papayas: the Mexican variety and the Hawaiian variety. Hawaiian papayas (also known as Solo) are usually found in supermarkets: they’re pear shaped, weighing a pound, and have a yellow skin when ripe, with the flesh being orange or pinkish. Mexican papayas can be found in supermarkets in South America and are much larger than the Hawaiian, weighing up to 20 pounds, despite being less tasty than their Hawaiian counterparts Esminger M. K. J et al. (Bayer, Ma, & Stockigt, 2004).



Figure 3
Papaya Seeds: They Have a Peppery Taste and Can Be Ground and Used as a Substitute for Black Pepper
Ensminger A H.

Papaya seeds are edible and have a peppery, bitter flavor. They are sometimes used in salads and can even be used as a substitute for black pepper Figure 3 Francois (Balbontin, et al., 2010). Papayas have been used for centuries by native Indians as a remedy for indigestion and digestive problems: its content in papain seems to reduce the symptoms of inflammation and speed up the recovery Francois (Balbontin, et al., 2010). Papaya leaves are very large, often being 50-70 cm diameter, and have seven lobes. Papayas were the first fruit to have their genome deciphered, and were the first genetically modified fruit for human consumption (they were enhanced in 1998 to be immune to the ringspot virus, which threatened papaya crops. Balbontín, Gaete-Eastman, Vergara, Herrera, & Moya-León, 2007). In India and Pakistan, green (unripe) papayas have been used for centuries as a folk remedy for abortion and contraception. These uses have been later confirmed by research, and today it is advised that pregnant women do not consume large amounts of green papayas. The ripe fruit is safe and does not cause problems Francois (Balbontin, et al., 2010). The leaves of the plant are steamed and eaten in Asia like spinach, while the green fruit is often used in Thai salads. Leaves are also used for tea, used in folk medicine to treat malaria (although medical research has not confirmed its protective effects). During the filming of *Indiana Jones and the Temple of Doom*, Harrison Ford was treated for a ruptured disc incurred during filming by having papain injected into his back (Molteni A Balbontín, Gaete-Eastman, Vergara, Herrera, & Moya-León, 2007).

2. HEALTH BENEFITS OF PAPAYA

Papayas offer not only the luscious taste and sunlit color of the tropics, but are rich sources of antioxidant nutrients such as carotenes, vitamin C and flavonoids; the B vitamins, folate and pantothenic acid; and the minerals,

potassium and magnesium; and fiber. Together, these nutrients promote the health of the cardiovascular system and also provide protection against colon cancer. In addition, papaya contains the digestive enzyme, *papain*, which is used like bromelain, a similar enzyme found in pineapple, to treat sports injuries, other causes of trauma, and allergies.

2.1 Protection Against Heart Disease

Papaya's may be very helpful for the prevention of atherosclerosis and diabetic heart disease. Papayas are an excellent source of vitamin C as well as a good source of vitamin E and vitamin A (through their concentration of pro-vitamin A carotenoid phyto nutrients), three very powerful antioxidants. These nutrients help prevent the oxidation of cholesterol. Only when cholesterol becomes oxidized it is able to stick to and build up in blood vessel walls, forming dangerous plaques that can eventually cause heart attacks or strokes. One way in which dietary vitamin E and vitamin C may exert this effect is through their suggested association with a compound called Paraoxonase, an enzyme that inhibits LDL cholesterol and HDL cholesterol oxidation Binns CW (Cho, Seddon, Rosner, Willett, Hankinson, 2004). Papayas are also a good source of fiber, which has been shown to lower high cholesterol levels. The folic acid found in papayas is needed for the conversion of a substance called homocysteine into benign amino acids such as cysteine or methionine. If unconverted, homocysteine can directly damage blood vessel walls and, if levels get too high, is considered a significant risk factor for a heart attack or stroke Binns CW (Cho, Seddon, Rosner, Willett, Hankinson, 2004).

2.2 Promotes Digestive Health

The nutrients in papaya have also been shown to be helpful in the prevention of colon cancer. Papaya's fiber is able to bind to cancer-causing toxins in the colon and keep them away from the healthy colon cells. In addition, papaya's folate, vitamin C, beta-carotene, and vitamin E have each been associated with a reduced risk of colon cancer. These nutrients provide synergistic protection for colon cells from free radical damage to their DNA. Increasing your intake of these nutrients by enjoying papaya is an especially good idea for individuals at risk of colon cancer Baybutt RC (Cantin, Moreno, & Gogorcena, 2009).

2.3 Anti-Inflammatory Effects

Papaya contains several unique protein-digesting enzymes including *papain* and *chymopapain*. These enzymes have been shown to help lower inflammation and to improve healing from burns. In addition, the antioxidant nutrients found in papaya, including vitamin C, vitamin E, and beta-carotene, is also very good at reducing inflammation. This may explain why people with diseases that are worsened by inflammation, such as asthma, osteoarthritis, and

rheumatoid arthritis, that the severity of their condition is reduced when they get more of these nutrients Baybutt RC (Cantin, Moreno, & Gogorcena, 2009).

2.4 Immune Support

Vitamin C and vitamin A, which is made in the body from the beta-carotene in papaya, are both needed for the proper function of a healthy immune system. Papaya may therefore be a healthy fruit choice for preventing such illnesses as recurrent ear infections, colds and flu Rebecca (Ensminger, & Esminger, et al., 1986).

2.5 Protection Against Macular Degeneration

Mother's especially mentions to children that taking carrots would keep your eyes bright as a child, but as an adult, it looks like fruit is even more important for keeping your sight. Data reported in a study published in the *Archives of Ophthalmology* indicates that eating 3 or more servings of fruit per day may lower your risk of age-related macular degeneration (ARMD), the primary cause of vision loss in older adults, by 36%, compared to persons who consume less than 1.5 servings of fruit daily. Its reported already which involved over 110,000 women and men, researchers evaluated the effect of study participants consumption of fruits; vegetables; the antioxidant vitamins A, C, and E; and carotenoids on the development of early ARMD or neovascular ARMD, a more severe form of the illness associated with vision loss. While, surprisingly, intakes of vegetables, antioxidant vitamins and carotenoids were not strongly related to incidence of either form of ARMD, fruit intake was definitely protective against the severe form of this vision-destroying disease. Three servings of fruit may sound like a lot to eat each day, but papaya can help you reach this goal. Add slices of fresh papaya to your morning cereal, lunch time yogurt or green salads. Cut a papaya in half and fill with cottage cheese, crab, and shrimp or tuna salad. For an elegant meal, place slices of fresh papaya over any broiled fish Symmons DP (Clifford, 1999).

2.6 Protection Against Rheumatoid Arthritis

While studies suggested that high doses of supplemental vitamin C makes osteoarthritis, a type of degenerative arthritis that occurs with aging, worse in laboratory animals, another indicates that vitamin C-rich foods, such as papaya, provide humans with protection against inflammatory polyarthritis, a form of rheumatoid arthritis involving two or more joints. The findings, presented in the *Annals of the Rheumatic Diseases* were drawn from a study of more than 20,000 subjects and focused on subjects who developed inflammatory polyarthritis and similar subjects who remained arthritis-free during the follow-up period. Subjects who consumed the lowest amounts of vitamin C-rich foods were more than three times more likely to develop arthritis than those who consumed the highest amounts Symmons DP (Clifford, 1999).

2.7 Promote Lung Health

If you or someone you love is a smoker, or if you are frequently exposed to secondhand smoke, then making vitamin A-rich foods, such as papaya, part of your healthy way of eating may save your life, suggests research conducted at Kansas State University. While studying the relationship between vitamin A, lung inflammation, and emphysema, Richard Baybutt, associate professor of nutrition at Kansas State, made a surprising discovery: a common carcinogen in cigarette smoke, benzo (a) pyrene, induces vitamin A deficiency. Baybutt's earlier research had shown that laboratory animals fed a vitamin A deficient diet developed emphysema. His latest animal studies indicate that not only does the benzo (a) pyrene in cigarette smoke cause vitamin A deficiency, but that a diet rich in vitamin A can help counter this effect, thus greatly reducing emphysema Rakhimov MR (Ensminger, Ensminger, Kondale, & Robson, 1983).

Baybutt believes vitamin A's protective effects may help explain why some smokers do not develop emphysema. "There are a lot of people who live to be 90 years old and are smokers," he said. "Why? Probably because of their diet... The implications are that those who start smoking at an early age are more likely to become vitamin A deficient and develop complications associated with cancer and emphysema. And if they have a poor diet, forget it." If you or someone you love smokes, or if your work necessitates exposure to second hand smoke, protect yourself by making sure that at least one of the World's Healthiest Foods that are rich in vitamin A, such as papaya, is a daily part of your healthy way of eating Baybutt RC (Cantin, Moreno, & Gogorcena, 2009).

2.8 Papaya and Green Tea Team Up to Prevent Prostate Cancer

Choosing to regularly eat lycopene-rich fruits, such as papaya, and drink green tea may greatly reduce a man's risk of developing prostate cancer, suggests research published the *Asia Pacific Journal of Clinical Nutrition* (Jian, Lee AH, et al., 2007; Dosil-Díaz, Ruano-Ravina, Gestal-Otero, & Barros-Dios, 2008).

In this case-control study involving 130 prostate cancer patients and 274 hospital controls, men drinking the most green tea were found to have an 86% reduced risk of prostate cancer compared, to those drinking the least Rakhimov MR (Da Cunha, et al., 2004). A similar inverse association was found between the men's consumption of lycopene-rich fruits and vegetables such as tomatoes, apricots, pink grapefruit, watermelon, papaya, and guava. Men who most frequently enjoyed these foods were 82% less likely to have prostate cancer compared to those consuming the least lycopene-rich foods Jian L, Lee AH, Rakhimov MR et al (Dosil-Díaz, Ruano-Ravina, Gestal-Otero, & Barros-Dios, 2008).

Regular consumption of both green tea and foods rich in lycopene resulted in a synergistic protective

effect, stronger than the protection afforded by either, the researchers also noted.

Practical Tips: Get in the habit of drinking green tea and eating lycopene-rich foods Jian L, Lee AH, et al ((Dosil-Díaz, Ruano-Ravina, Gestal-Otero, & Barros-Dios, 2008; Da Cunha, et al., 2004).

- Take a quart of iced green tea to work and sip throughout the day or take it to the gym to provide prostate protection while replenishing fluids after your workout.

- Pack a ziploc bag of apricots and almonds in your briefcase or gym bag for a handy snack.

- Start your breakfast with a half grapefruit or a glass of papaya or guava juice.

- Add papaya to any smoothie or fruit salad or use as a delectable garnish for fish.

- For a delicious summer lunch, cut a papaya in half, scoop out the seeds, sprinkle with lime juice and top with cottage cheese, a fresh mint leaf, and roasted almonds.

- Begin lunch or dinner with some spicy tomato juice on the rocks with a twist of lime. Snack on tomato crostini: in the oven, toast whole wheat bread till crusty, then top with tomato sauce, herbs, a little grated cheese, and reheat until the cheese melts.

- Top whole wheat pasta with olive oil, pine nuts, feta cheese and a rich tomato sauce for lunch or dinner.

3. OTHER BENEFITS OF PAPAYA AND ITS CONTENTS

3.1 Industrial Applications of Papain

The papain present in the latex of *Carica papaya* has been extensively studied and was found to be an enzyme of industrial use and of high research interest. Among the major applications of papain are its use in the food industry, beer clarification, meat tenderizing, Preparation of protein hydrolysates and others Jonas Contiero (Guorong, Mingjun, Fengwang, & Dong, 2009).

3.2 Wound Healing Activity of Carica Papaya

Carica Papaya is used as food or as medication in folk medicine; papain is the active principle in carica papaya that exerts the ulcer-protective effect reduces gastric acid secretion induced by histamine in rats. Carica papaya fruit extract possess antibacterial antioxidant anti-inflammatory activity antifertility antihypertensive agent chronic skin ulcer therapy and diuretic effects.

Green papaya is rich in two enzymes that have very strong digestive properties: papain and chymopapain. Papain, the enzyme used in commercial has the ability to dissolve dead tissue without damaging living cells. Accuzyme, a debriding ointment that contains papain and urea, is available to debride necrotic tissue and liquefy slough in a variety of acute and chronic lesions. Chymopapain was also used in the healing and recovery

of surgical wounds Salmah. I (Gayosso, Yahia, Martínez-Téllez, & González-Aguilar, 2010).

4. METHODOLOGIES

4.1 Response Surface Methodology

World demand for fruit juices, including exotic or tropical juices is increasing. Value added products from underutilized fruits like papaya (*Carica papaya* L.) and jackfruit (*Artocarpus heterophyllus* Lam.) can be commercially exploited due to their high nutritive value. The fruit juices of papaya and jackfruit can also compete either as individual juice or as blends. Although there are reports on enzymatic liquifaction of jackfruit and papaya, little information is available on their optimization with respect to operating parameters. In order to obtain juice from jackfruit and papaya pulp, pectinase enzyme is added which reduces the viscosity of the pulp and facilitates separation of the juice from the pulp. The enzymatic liquefaction is reported to be influenced by the enzyme concentration, incubation time and hydrolysis temperature Rakhimov MR (Ensminger, Ensminger, Kondale, & Robson, 1983). A graphical optimization technique was used to minimize alcohol insoluble solids (AIS) and to increase juice yield of jackfruit and papaya respectively. When many factors and interactions influence the desired response, surface methodology (RSM) is an effective tool for optimizing the process. RSM is a statistical method that uses quantitative data from appropriate experimental designs to determine and simultaneously evaluate multivariate equations Ramesh Yadav Avula (Fortin & Francois, 1996).

The following can be studies using RSM

- 1) Study the effect of enzyme concentration, incubation time and hydrolysis temperature on
 - i) reduction in AIS during liquefaction of jackfruit
 - ii) increase in juice yield in case of papaya and
- 2) optimize the enzymatic liquefaction of papaya and jackfruit pulp.

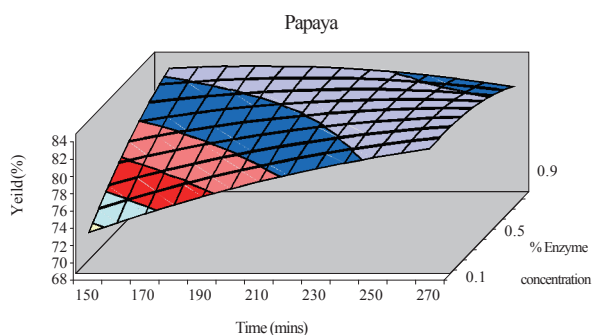


Figure 4
Response Surface Graph Showing the Effect of Enzyme Concentration and Incubation Time on % Juice Yield of Papaya Ramesh Y. A.

Table 3
Statistical Analysis of the Comparison of Experimental Values

Fruit	RSMD	SD	E (%)
Papaya	0.551	0.679	0.76
Jackfruit	0.018	0.021	0.74

*Values are the mean of triplicate determinations.

The effect of the enzyme concentration, incubation time and incubation temperature seems to be significant in case of liquefaction of jackfruit and papaya using response surface methodology. The different conditions (time, temperature and enzyme concentration) for enzyme treatment revealed that, all these variables markedly affect the parameter under study. However, enzyme liquifaction does not have any significant effect on the nutritive properties of the juice. To explore whether the predictive model from RSM could be applied to scale up the process, the study was carried out at pilot plant level. The model equation developed for yield and AIS could predict values close to the experimental ones. The response surface methodology provides insight into the interaction and identifies the optimum combination of variables. The methodology developed in this research can also be extended to other fruits as well Ramesh Yadav Avula (Fortin & Francois, 1996).

4.2 Purification of Papain From Fresh Latex of *Carica Papaya*

Reported in literature researchers (Guorong, Mingjun, Fengwang, & Dong, 2009) developed a process for the purification and isolation of papain in the native crystalline state from fresh latex. This method was later modified using commercially available dry latex and has been the classical method for papain preparation for many years, with some later modifications. Aqueous extracts of *Carica papaya* latex contain some cysteine proteinases that can be separated by ion exchange chromatography, and fully active forms can also be obtained by covalent chromatography using thiol-disulfide exchange. The kinetics and ionization of the catalytic site of papain obtained by different methods (Cys-S-/His-Im+H formation) are a matter of controversy. Studies carried out by one of the major groups specializing in research on the cysteine-proteinase family from the latex of *Carica papaya* have demonstrated the importance of the use of reversible inhibitors during their isolation and manipulation (Brocklehurst et al., 1981). The researchers also emphasized that the multiple ionizations occurring in chymopapain and papain may be a general phenomenon for the cysteine-proteinase family (Thomas et al., 1994). A new method was reported later, on the development of a method for the purification and crystallization of native papain from fresh latex (Monti, 1983; Guorong, Mingjun, Fengwang, & Dong, 2009), which differs from the classical methods described in the literature. The

method showed that papain precipitates spontaneously at low temperatures, presenting a high level of purity and excellent catalytic activity in comparison to classical methods of Kimmel & Smith, 1954 (Guorong, Mingjun, Fengwang, & Dong, 2009).

Use of the Model Three-Dimensional Structure

The model of the three-dimensional structure of chymopapain M, built as part of the present work (Figure 5), and the superposition of this and the crystal structure of papain demonstrate the presence in chymopapain M of many of the kinetically and mechanistically relevant structural features present in the papain molecule, and reveal a number of interesting differences. Thus common features (chymopapain M numbering with papain numbering in parentheses where it differs) include: (i) the three disulphide bonds Cys-22-Cys-63, Cys-56-Cys-95 and Cys-153-Cys-204 (Cys-153-Cys-200) involved in the maintenance of the folded structure; (ii) the Trp-shielded nucleophilic/acid-base and oxyanion hole systems of the catalytic site, Trp-181 (Trp-177), Cys-25, His-159, Asn-179 (Asn-175) and Gln-19; (iii) the potential electrostatic influences close to the catalytic site described 17-Yahia, M. E. (Gayosso, Yahia, Martínez-Téllez, & González-Aguilar, 2010; Jian, Lee, & Binns, 2007; Jarvik, et al., 2002; Jian, Lee, & Binns, 2007) (iv) the hydrogen-bond donor/acceptor systems considered to bind the non-scissile P1-P2 amide bond of substrates within the active-centre cleft, the backbone NH of Gly-66 and the backbone C=O of Asp-158; (v) many of the residues in or near to the hydrophobic pocket of the S2 subsite (the principal binding site of papain; Figure 5), Tyr-61, Tyr-67, Val-133, Val-157, Ala-160 and Ser-209 (Ser-205).

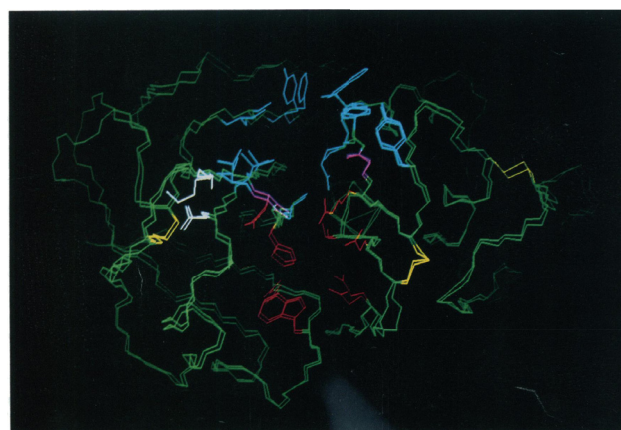


Figure 5
Three Dimensional Structure of Chymopapain Yahia, M. E

5. CHEMISTRY AND MECHANISM OF *CARICA PAPAYA*

During few decades, the consumption of fruits and vegetables has increased considerably due to their benefits

for good health. Many biochemical and epidemiological studies have demonstrated that fruits and vegetables contribute to the reduction of several diseases, including cardiovascular, neurological, and carcinogenic illnesses Yahia, M. E. (Jian, Lee, & Binns, 2007). These benefits have been attributed, at least in part, to the amount of antioxidant compounds present in these foods, which reduce the oxidative stress produced by free radicals, and in consequence, cellular damage. Some of the most important antioxidant compounds present in fruits and vegetables include polyphenols, carotenoids, vitamin C, vitamin A, vitamin E, carbohydrates, fiber, fats, and protein Yahia, M. E. (Jian, Lee, & Binns, 2007). Phenolic compounds are aromatic metabolites of plants secondary metabolism that have a common structure with an aromatic ring with at least one hydroxyl group, which provides the ability to neutralize reactive species, helping the body to protect itself from oxidative stress Barros-Dios, J. M. (Jian, Lee, & Binns, 2007). Additionally, phenols contribute to fruits' color and taste which is well documented. In several fruits such as papaya, the content of carotenoids increases with ripening Wall, M. M (Li, Molteni, Latkovich, Castellani, & Baybutt, 2003). Lycopene, β -cryptoxanthin, and β -carotene are the main carotenoids that have been identified in papaya Lopes Teixeira, S. (Li, et al., 2006). Vitamin C (ascorbic acid) is a hydrophilic vitamin present in fruit. It plays an important role because it is required for several metabolic processes like development of tissues and production of hormones Cortés, M. (Laura, Gayosso, Elhadi, Yahia, & Adolfo, 2011) and is also considered a powerful antioxidant reducing oxidative stress Dong, L. (Mahmood, Sidik, & Salmah, 2005). In addition, it has been observed that vitamin C can act synergically with other vitamins and play an important role to regenerate vitamin E. Recently, its reported the physiological and biochemical changes that occur during ripening of "Maradol" papaya and its antioxidant status González-Aguilar, G.A (Marelli, Silva, Paes, & Lopes Teixeira, 2008).

Vitamin C (ascorbic acid) is a hydrophilic vitamin present in fruit. It plays an important role because it is required for several metabolic processes like development of tissues and production of hormones Cortés, M (Laura, Gayosso, Elhadi, Yahia, & Adolfo, 2011) and is also considered a powerful antioxidant reducing oxidative stress Dong, L (Mahmood, Sidik, & Salmah, 2005). In addition, it has been observed that vitamin C can act synergically with other vitamins and play an important role to regenerate vitamin E. Phenolic compounds were also identified in saponified and nonsaponified extracts of papaya skin by HPLC-ESI-MS. The major phenolic compounds identified in saponified extracts were hydroxycinnamic acid sugar derivatives, while the non-saponified extracts showed only traces of these compounds in an acylated form (data not shown). Caffeic acid was identified tentatively as a [M-H]-deprotonated

molecule (m/z 179), with loss of the CO₂ group in the form of negative ion, with an UV spectrum (λ_{max} =280, 320 nm) in a retention time (RT) of 16.8 min. p-Coumaric acid was tentatively identified as a [M-H]-deprotonated molecule (m/z 163) in a RT of 19.04 min and yielded ion fragments at m/z 119 and 153. Ferulic acid was tentatively identified according to its UV spectrum (λ_{max} =280, 320 nm) as a [M-H]-deprotonated molecule (m/z 193), with a RT of 22.4 min, and yielded ion fragments at m/z 117, 134, 149, and 179 (Figure 6). Profile of phenolic compounds but not concentration coincides with the first report on the identification of phenolics in "Maradol" papaya skin made Gonzalez-Aguilar, G. (Ma, Koep, Panjkar, Fritzch, Stockigt, 2005). Phenolic compounds have been reported to have antiradical, antimutagenic, and anticarcinogen properties and protect plants from UV radiation Gogorcena, Y (Puente, Pinto-Muñoz, Castro, & Cortés, 2010).

Esterified form of Quinic acid also known as chlorogenic acid Clifford, M. N (Pattison, et al., 2004) found in many fruits, vegetables, and coffee Campos, M. M. observed that caffeic acid and its derivatives exert anti-inflammatory activity both in vitro and in vivo, and this activity was due in part to the removal of nitric oxide (NO) and its ability to modulate the expression of INOS (inducible nitric oxide synthase). p-Coumaric acid is an intermediate in the synthesis of phenyl propanoids and has been shown to have antioxidant properties, lowers cholesterol, and provides a defense mechanism against atherosclerosis Vallyathan, V (Rakhimov, 2000,) p-coumaric acid oral administration (317 mg/day for 30 days) inhibited the oxidation of LDL, reduced serum cholesterol levels and did not affect HDL levels, and contributed considerably to the antioxidant capacity, which is directly related to the removal of ROS.

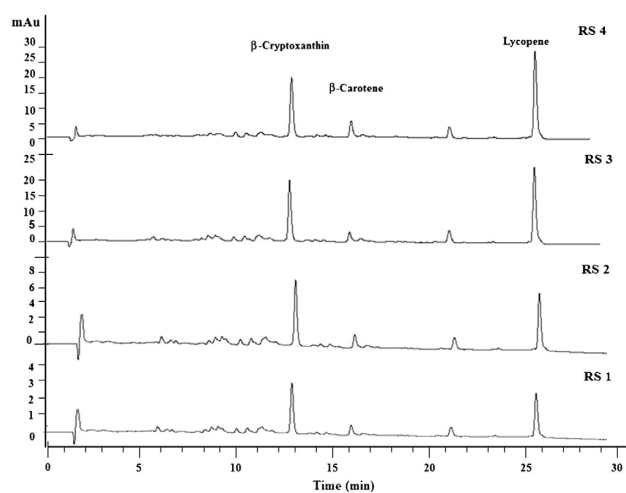


Figure 6
HPLC Carotenoids Chromatograms at 450 nm in Papaya Flesh (Carica papaya L. cv. Maradol) in Four Stages of Ripeness. RS1 (0-25% yellow), RS2 (N25 and 50% yellow), RS3 (N50 and 75% yellow), and RS4 (N75 and 100% yellow) González-Aguilar

Alcohol acyltransferase (AAT), catalyzes the esterification reaction between alcohols and acyl-CoAs, is the key enzyme involved in ester biosynthesis in this species M.A.Moya-León (Rubens, Carmelita, Henrique, & Jonas, 2000). Recently, a gene encoding for an alcohol acyltransferase (VpAAT1) has been isolated and characterized in ripening *carcifera* papaya fruit M.A.Moya-León (Rubens, Carmelita, Henrique, & Jonas, 2000).

The first member from the BAHD super family possesses a crystal structure is vinorine synthase, an acetyl transferase from *Rauvolfia serpentina* J. Stockigt (Rivera, Yahia, & Gonzalez-Aguilar, 2010). Members of the BAHD superfamily share the HXXXD motif, located in the middle of the protein sequence, which is highly conserved in higher plant and yeasts González-Aguilar. The substitution of the histidine and aspartic residues from this motif causes the loss of enzyme function in vinorine synthase J. Stockigt (Souleyre, Greenwood, Friel, Karunairatnam & Newcomb, 2005), which suggests that it could be involved in the transfer of the acyl group from acyl-CoA towards the alcohol. The understanding of the catalytic properties of the enzymes involved in the production of volatiles in a particular fruit could allow the design of additional strategies to improve its flavor during storage, shipping, marketing or processing.

belonging to the BAHD super family Moya-León M. A. (Rubens, Carmelita, Henrique, & Jonas, 2000). A large number of acyl transferases have been described in plants, whereas in fruit species such as melon and apple a small gene family has been identified J.C. Pech, R.D. Newcomb, H. Shu (Wojdyło, Oszmianski, & Laskowski, 2009; Wall, 2006; Wood, 1988). The BAHD superfamily members have been divided into three subfamilies (I, II and III) H. Shu (Wood, 1988) and VpAAT1 has been clustered into subgroup III Moya-León M. A. (Rubens, Carmelita, Henrique, & Jonas, 2000). Members of subfamily III have been described for their great capacity to produce benzyl acetate E. Pichersky (Yahia, 2010), and interestingly, benzyl acetate has not been described as an aroma volatile in papaya *carcifera* fruit (Attar, 2004), although the recombinant protein is able to synthesize this ester.

While understanding the structural and functional characteristics, the 3D structure of VpAAT1 protein was built by homology modelling and molecular dynamic simulations E. Pichersky (Yahia, 2010). The model obtained fulfils the structural characteristics proposed for the BAHD superfamily, including the solvent channel in where the active site is located, and the globular shape composed by two equally sized domains connected by an extensive loop (residues 210-232). The VpAAT1 structure presented in this work reported by explains the functional importance of a residue located in loop13 between helix 5 and strands 7, and directly situated in the center of the solvent channel. This structural arrangement allows the incorporation of different acyl-CoAs and alcohols as substrate to approach the active site, at the front face (acyl-CoA binding) and the backface (alcohols binding) of the enzyme. In the HTMSD motif, the Asp170 is located close to His 166 and it is part of the active site. The importance of the residues His and Aspin the HXXXD motif has also been demonstrated by chemical modification and site-directed mutagenesis experiments for other members of the BAHD superfamily Vallyathan, V (Rakhimov, 2000). The BAHD super family enzymes might therefore have a similar conformation of the catalytic His and use a similar reaction mechanism to that proposed for VpAAT1. Molecular docking analysis indicates that interaction between VpAAT1 enzyme with acetyl-CoA and benzylalcohol showed the most favorable binding energy, and there combinant protein displayed a high activity towards the synthesis of benzylacetate, so the 3D models show specific interactions between the substrates benzylalcohol and acetyl-CoA and key aminoacid residues in the active site, and thus these interactions are consistent with the previously reported experimental data concerning the catalytic activity of VpAAT1 Baybutt RC (Cantin, Moreno, & Gogorcena, 2009). Furthermore, the analysis performed supports the hypothesis that VpAAT1 enzyme shares similar structural and functional characteristics to

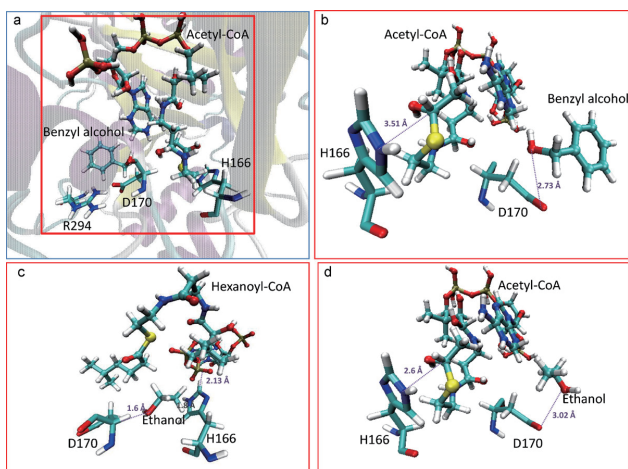


Figure 7
Ligand Binding Analysis Based on the Refined VpAAT1 Model. (a) The 3D structure of acetyl-CoA benzyl alcohol VpAAT1 complex is shown. (b) Docking of benzyl alcohol and acetyl-CoA to VpAAT1 model. (c) Docking of ethanol and hexanoyl-CoA to VpAAT1 model. (d) Docking of ethanol and acetyl-CoA to VpAAT1 model (Dash lines indicate distance between atoms E. Pichersky.)

Papaya *carcifera* is a climacteric fruit that develops an interesting and characteristic aroma during ripening, which is mainly due to esters Moya-León M. A. (Sharkawy, et al., 2005), which are synthesized by alcohol acyl transferases. A gene (VpAAT1) has been isolated from papaya *carcifera* fruit and its protein sequence shares all the conserved regions described for other acyl transferases

members of the acyl transferase subfamily III with high activity for the production of benzylacetate H. Shu (Wood, 1988). Therefore, the fact that papaya *carcifera* fruit does not produce benzylacetate maybe due to the absence of substrates during fruit ripening and not to the inability of VpAAT1 protein to interact with the substrates.

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CONCLUSIONS

Fruits are regarded as crowning glory of fibre, minerals. The mini review highlights about the health benefits of papaya which contains essential nutrients and minerals which are the back bone of human survival. While the emerging process have to be replaced with various fruits and vegetables owing to the limitations of drugs, and pills which are manufactured by conventional chemical routes? Among the fruits papaya have been selected due to its various health benefits, protection against heart disease, promotes digestive health, anti-inflammatory effects, immune support, protection against macular degeneration, protection against rheumatoid arthritis, wound healing property of *papaya cercia* and industrial applications. Since they are in the natural form, account for largest part of water and 100% bad cholesterol free, it's much easier for the body to process and absorb the vitamins and minerals from the fresh fruit. The chemistry and mechanism, of papaya fruit is well understanding i.e co-esterase enzyme present in ripen papaya fruit under goes benzyl alcohol esterification reaction when using this enzyme. From this we can say that a new route is developed for esterification reactions. Papaya is a value added commodity for the betterment of society.

REFERENCES

Attar, S. C, Sadia, G. A, Mysore, N. R, Ramesh, Y. A, Mysore, N. R., & Ramesh, S. R. (2004). Optimization of enzymatic liquefaction of papaya (*Carica papaya* L.) and jackfruit (*Artocarpus heterophyllus* Lam.) pulp using response surface methodology. *Food, Agriculture & Environment*, 2(2), 108-113.

Auria, J. D., Chen, F., & Pichersky, E. (2002). Characterization of an acyl transferase capable of synthesizing benzylbenzoate and other volatile esters in flowers and damaged leaves of *Clarkia breweri*. *Plant Physiol.*, 130, 466-476.

Balbontin, C, Gaete-Eastman, C, Fuentes, L, Figueroa, C. R., & Herrera, R., Manriquez D., Latche A., Pech J. C, Moya-León M. A. (2010). VpAAT1, a gene encoding an alcohol

acyltransferase, is involved in ester biosynthesis during ripening of mountain papaya fruit. *J. Agric. Food Chem.*, 58, 5114-5121.

- Balbontín, C., Gaete-Eastman, C, Vergara, M., Herrera, R., & Moya-León, M. (2007). Treatment with 1-MCP and the role of ethylene in aroma development of mountain papaya fruit. *Postharvest Biol. Technol.*, 43, 67-77.
- Baybutt, R C, Hu L, & Molteni, A. (2000). Vitamin A deficiency injures lung and liver parenchyma and impairs function of rat type II pneumocytes. *J. Nutr.*, 130(5),1159-65. PMID: 10801913.
- Bayer, A., Ma, X. Y., & Stockigt, J. (2004). Acetyltransfer in natural product biosynthesis—functional cloning and molecular analysis of vinorine synthase, *Bioorg. Med. Chem.*, 12, 2787-2795.
- Cantin, C. M., Moreno, M. A., & Gogorcena, Y. (2009). Evaluation of the antioxidant capacity, phenolic compounds, and vitamin c content of different peach and nectarine [*Prunus persica* (L.) Batsch] breeding progenies. *Journal Agricultural of Food Chemistry*, 57, 4586-4592.
- Cho, E., Seddon, J. M., Rosner, B, Willett, W. C., Hankinson, S. E. (2004, June). Prospective study of intake of fruits, vegetables, vitamins, and carotenoids and risk of age-related maculopathy. *Arch Ophthalmol.*, 122(6),883-92. PMID:15197064.
- Clifford, M. N. (1999). Chlorogenic acids and other cinnamates—nature, occurrence and dietary burden. *Journal of the Science of Food and Agriculture*, 79, 362-372.
- [10] Da Cunha, F. M., Duma, D., Assreuy, J., Buzzi, F. C., Niero, R., Campos, M. M., et al. (2004). Caffeic acid derivatives: in vitro and in vivo anti-inflammatory properties. *Free Radical Research*, 38, 1241-1253.
- Dosil-Díaz, O., Ruano-Ravina, A., Gestal-Otero, J. J., & Barros-Dios, J. M. (2008). Consumption of fruit and vegetables and risk of lung cancer: A case-control study in Galicia, Spain. *Nutrition*, 24(5), 407-413.
- Ensminger, A. H, & Esminger, M. K. J. et. al. (1986). *Food for health: A nutrition encyclopedia*. Clovis, California: Pegus Press. PMID: 15210.
- Ensminger, A. H, Ensminger, M. E, Kondale, J. E., & Robson, J. R. K. (1983). *Foods & nutriton encyclopedia*. Clovis, California: Pegus Press.
- Fortin, C., & Francois, K. (1996). *The visual foods encyclopedia*. New York: Macmillan.
- Gayosso, S., Yahia L. E., Martínez-Téllez E. M., & González-Aguilar M. A. (2010). Effect of maturity stage of papaya Maradol on physiological and biochemical parameters. *American Journal of Agricultural and Biological Sciences*, 5(2), 199-208.
- Guorong, D., Mingjun, L., Fengwang, M., & Dong, L. (2009). Antioxidant capacity and the relationship with polyphenol and vitamin C in *Actinidia* fruits. *Food Chemistry*, 113, 557-562.
- Jarvik, G. P., Tsai N. T, & McKinstry, L. A., et al. (2002). Vitamin C and E intake is associated with increased

- paraoxonase activity. *Arterioscler Thromb Vasc Biol Aug 1*, 22(8), 1329-1333.
- Jian, L., Lee A. H., & Binns, C. W. (2007). Tea and lycopene protect against prostate cancer. *Asia Pac J Clin Nutr.*, 16 Suppl. 1, 453-457. PMID: 17392149.
- Jian, L., Lee, A. H., & Binns, C. W. (2007). Tea and lycopene protect against prostate cancer. *Asia Pacific Journal of Clinical Nutrition*, 16, Suppl. 453-7.
- Laura, E., Gayosso, G. S., Elhadi, M., Yahia, G., & Adolfo, G. A. (2011). Identification and quantification of phenols, carotenoids, and vitamin C from papaya (*Carica papaya* L., cv. Maradol) fruit determined by HPLC-DAD-MS/MS-ESI Food Research International. doi:10.1016/j.foodres.2010.12.001
- Li, D., Xu Y, Xu, G., Gu, L., Li, D., & Shu, H. (2006). Molecular cloning and expression of a gene encoding alcohol acyltransferase (MdAAT2) from apple (cv. Golden Delicious). *Phytochemistry*, 67, 658-667.
- Li, T, Molteni, A, Latkovich, P, Castellani, W, & Baybutt, R. C. (2003). Vitamin A depletion induced by cigarette smoke is associated with the development of emphysema in rats. *J. Nutr.*, 133(8), 2629-2634. PMID: 12888649.
- Ma, X., Koep J., Panjekar, S., Fritzch, G., & Stockigt, J. (2005). Crystal structure of vinorine synthase, the first representative of the BAHD superfamily. *J. Biol. Chem.*, 280, 13576-13583.
- Mahmood, A. A, Sidik, K., & Salmah, I. (2005). Wound Healing Activity of *Carica papaya* L. Aqueous leaf extract in rats. *Int. Journal of Molecular Medicine and Advance Sciences*, 1(4), 398-401.
- Marelli, de S., Silva, F. L., Paes, C. J. B., & Lopes Teixeira, S. (2008). LAscorbic acid, β -Caroteno and lycopene content in papaya fruits (*Carica papaya*) without physiological skin freckles. *Science Agriculture*, 65(3), 246-250.
- Pattison, D. J., Silman, A. J., Goodson, N. J., Lunt, M, Bunn, D, Luben, R, Welch, A., Bingham, S, Khaw, K. T., Day, N., & Symmons, D. P. (2004, July). Vitamin C and the risk of developing inflammatory polyarthritis: Prospective nested case-control study. *Ann Rheum Dis.*, 63(7), 843-847. PMID: 15194581.
- Puente, L. A., Pinto-Muñoz, C. A., Castro, E. S., & Cortés, M. (2010). The multiple properties of a highly functional fruit: A review. *Food Research International*. doi: 10.1016/j.foodres.2010.09.034
- Rakhimov, M. R. (2000, May-Jun). Pharmacological study of papain from the papaya plant cultivated in Uzbekistan (Article in Russian). *Eksp Klin Farmakol*, 63(3), 55-57.
- Rivera, P., Yahia, D. M., & Gonzalez-Aguilar, G. (2010). Phenolic and carotenoid profiles of papaya fruit (*Carica papaya* L.) and their contents under low temperature storage. *Journal of the Science of Food and Agriculture*, 90, 2358-2365.
- Rubens, M., Carmelita, A., Henrique, C. T., & Jonas, C. (2000). Purification of papain from fresh latex of *Carica papaya*. *Brazilian Archives of Biology and Technology*, 43(5), 501-507.
- Sharkawy, I. E., Manriquez, D., Flores, F. B., Regad, F., Bouzayen, M., Latche, A., & Pech J. C. (2005). Functional characterization of a melon alcohol acyl-transferase gene family involved in the biosynthesis of ester volatiles. Identification of the crucial role of a threonine residue for enzyme activity. *Plant Mol. Biol.*, 59, 345-362.
- Souleyre E. J., Greenwood D. R., Friel E. N., Karunairatnam S, & Newcomb R. D. (2005). An alcohol acyltransferase from apple (cv. Royal Gala), MpAAT1, produces esters involved in apple fruit flavor. *FEBS J.* 272, 3132-3144.
- The world's Healthiest Foods. Papaya. Retrieved from <http://www.whfoods.com/genpage.php?name=foodspice&dbid=47>
- Wall, M. M. (2006). Ascorbic acid, vitamin A, and mineral composition of banana (*Musa* sp.) and papaya (*Carica papaya*) cultivars grown in Hawaii. *Journal of Food Composition and Analysis*, 19, 434-445.
- Wojdyło, A., Oszmianski, J., & Laskowski, P. (2009). Polyphenolic compounds and antioxidant activity of new and old apple varieties. *Journal Agricultural of Food Chemistry*, 56, 6520-6530.
- Wood, R. (1988). *The whole foods encyclopedia*. New York, NY: Prentice-Hall Press. PMID: 15220.
- Yahia, M. E. (2010). The contribution of fruit and vegetable consumption to human health. In L. A. de la Rosa, E. Alvarez-Parrilla, & G. A. Gonzalez-Aguilar (Eds.), *Fruit and vegetable phytochemicals* (pp.3-51). USA: Wiley-Blackwell.
- Zang, L. Y., Cosma, G., Gardner, H., Shi, X., Castranova, V., & Vallyathan, V. (2000). Effect of antioxidant protection by p-coumaric acid on low-density lipoprotein cholesterol oxidation. *American Journal of Physiology Cell Physiology*, 279, 954-960.