

Phytochemical screening and bioactivity assessment of leaves and fruits extract of *Carica papaya*

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Abstracts: The consumption of fruits and vegetables has increased in recent years due to their health benefits as fruits and vegetables contain secondary metabolites, those has been reported to possess different pharmacological effects against many human ailments. In the current study antioxidants, antimicrobial and cytotoxic effects of leaves and fruit extracts of *Carica papaya* were evaluated. The antioxidant activities of plant extracts were carried out by using 2,2 – diphenyl-1- picrylhydrazyl. (DPPH), H₂O₂, 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid (ABTS) and reducing power assays and were compared with standards compounds (Ascorbic acid and Rutin). Antibacterial and antifungal activities of leaves and fruit extracts were assessed against four bacterial and fungal strains and also their minimum inhibitory concentration (MIC) values were calculated. Whereas for evaluation of cytotoxicity of plant extracts, brine shrimps cytotoxic assay was performed. Plant extracts were finally analyzed for phytochemicals by using UV/Visible spectrophotometer and High performance liquid chromatography (HPLC). Results indicates that plants extracts contained important compounds (phenols, flavonoids and other secondary metabolites) those have higher antioxidants and antimicrobial as well as lower proportion of MIC values. Whereas cytotoxic index of plant extracts were minor that specifies its appropriateness to use as a pharmaceutical materials probably be essential for drugs preparation. It is expected that such drugs could be lesser toxic and have lower cost as compared to drugs already available in market

Keywords: *Carica papaya*, leaves and fruit extracts, antioxidants, antimicrobial, HPLC, DPPH, ABTS, H₂O₂, secondary metabolites.

INTRODUCTION

In developing countries larger proportion of people are residing in rural areas and are using plant materials as home remedy against different ailments as reported by World Health Organization (WHO, 2012) which also documented significant pharmacological importance of different plants. However, ethno botanical information regarding their properties, safety and efficiency must be disseminating to human population (Ellof, 1998). According to information available in literature the interest of consumers is now focused on to use of products having natural antioxidants as compared to synthetic as well as to avoid the use of drugs having carcinogenic side effects after consumption (Velioğlu *et al.*, 1998). Many medicinal plants contain large amounts of antioxidants such as polyphenols, which can play an important role in adsorbing and neutralizing free radicals, quenching singlet and triplet oxygen, or decomposing oxidative reaction. The Plant source nutrients acquired substantial antioxidant capability that is associated with lesser mortality rates of many human diseases (Anderson *et al.*, 2001).

According to Chen (1992) battle of synthetic antibiotics

drugs against microorganism is not successful as many bacteria have genetic ability to show resistance for these drugs after couple of years and due to this new scenario hospitalized patients got suppressed immunity condition. Consequently, new infections can occur in hospitalized patients those could worsen the condition, resulting in high mortality rates. The fruits and vegetables contain several compounds those are reconsidered as anti-cytotoxic, antigen toxic and are able to reduce incidence of tumors. Therefore, understanding about health benefits and/or potential toxicity of these plants is important.

The common and easy method to detect cytotoxicity of plant materials is the brine shrimp assay. This bioassay is widely used in the evaluation of toxicity of heavy metals, pesticides, medicines especially natural plant extracts etc. (Pisutthanan *et al.*, 2004; McLaughlin *et al.*, 1991).

Carica papaya L. belongs to family Caricaceae is excessively distributed throughout the tropics and subtropics countries. It is a berry like fruit grow from ovary that is superior and its placentation is parietal (Kochhar, 1986). The leaves and fruits of papaya contained phenols, flavonoids, carotenoids, essential vitamins and minerals (Rahmat *et al.*, 2012). The *Carica latex* contained chitinase, glutamine cyclase and cysteine

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endopeptidases (Papain, chymopapain and caricain). Linalool in fruit pulp and alkaloids like carpaine, pseudo-carpaine, dehydrocarpaine I and II (Lim, 2012). Different parts of the papaya plants including fruits, leaves, stems, seeds and roots have long been used as ingredients in alternative medicines. The antioxidant properties of *Carica papaya* fruits is very useful and it is very helpful in boosting immune system of the body against reactive oxygen species. These destructive products are produced as a result of lipid oxidation in the human body. Reactive oxygen species (ROS) are presently considered as source for several human infections (Repetto and Llesuy, 2002; Rahmat *et al.*, 2004). Many tropical and subtropical countries are affected by dengue infections caused by viruses belong to the Flaviviridae family. Many reports are available in literature indicating that people affected by dengue fever are restored by use of Papaya leaf extracts. However, scientific proof about use of Papaya leaf extracts against dengue fever is still not reported. There for keeping in view the beneficial effects of leaves and fruit of *C. papaya* the present study was designed to assess its antioxidants, antimicrobial and cytotoxic effects of leaves and fruit extracts of *Carica papaya*.

MATERIALS AND METHODS

Collection and preparation of samples

Plant collection of *Carica papaya* was done from different areas of Rawalpindi, identified by ethno botanist and registered specimen (voucher no, 135) in UAAR-Ethno botanical Catalogue for future reference. The leaves and fruit samples were washed with water and 10% ethanol to get rid of any microbial contamination and shadow dried, followed by oven drying at 37°C and further ground (80 meshes) and stored in fine plastic bags for further uses at room temperature.

Preparation of plant extracts using polarity based fraction technique

Phytochemical analysis of different plant extracts was done according to already developed modified protocol in our lab. For preparation of plant extracts, 50 g of fruit and leaves samples of *Carica papaya* were separately placed in 500ml extraction flask and macerated using different solvents in polarity based manner with n-hexane, chloroform, ethanol, methanol and water at 1:10 of sample to solvent. Extraction procedure was repeated under closed incubation conditions of 37°C, 150 rpm for 24 hours in three cycles. Samples were filtered using cellulose filters of mesh size 1mm and evaporated using rotary evaporator under controlled conditions. Extracts were stored in closed amber vials at 4°C to prevent any further contamination.

Phytochemical analysis of *Carica papaya* samples

The leaves and fruit extracts were qualitatively analyzed and quantitative analysis of secondary metabolites was

further done using methods reported by Afzal *et al.* (2013), Harbone (1973) and Trease and Evans (1983). Total phenolic contents were evaluated from various extracts of *Carica papaya* (Kim *et al.*, 2003). Whereas, flavonoids contents of leaves and fruit extracts were quantified by using method reported by Hussain *et al.* (2012).

Chromatographic analysis

The ethanolic extracts of both fruits and leaves were found to have higher concentrations of total flavonoids. The extracts were further used for quantification of flavonoids (quercetin and rutin) by using HPLC (Shimadzu). About 20µl of sample was injected to reversed phase C-18 column at 40°C under isocratic elution, with methanol and water mixture (70:30). The flow rate of sample was 1 ml/min and retention time 20 min. Quercetin and rutin were used as standards and amount of flavonoids was monitored by UV/visible detector at 368 nm wavelength.

Antioxidant activities of leaves and fruit extracts of *Carica papaya*

The antioxidant potential of both leaves and fruits extracts were determined using modified protocols against different oxidants such as H₂O₂, DPPH, ABTS. To reduce Fe⁺³ ions into Fe⁺² ions by different extracts, reducing power assay was done as described by Yildirim *et al.* (2001). Scavenging ability was determined by using DPPH assay as reported by Moon and Shibamoto (2009) and using ABTS assay (Ashafa *et al.*, 2010). The activity of extracts to scavenge H₂O₂ was assessed on the basis of procedure published by Ruch *et al.* (1989). All experiments were run in triplicates and data was analyzed to determine percentage scavenging activity.

Determination of antimicrobial activity of extracts

Plant samples were screened to determine antibacterial potential by using agar well diffusion assay against four bacterial strains, *Staphylococcus aureus* (ATCC 6538), *Escherichia coli* (ATCC15224), *Klebsiella pneumonia* (MTCC618) and *Bacillus subtilis* (ATCC6633). Standard antibiotics (Cefixime and Roxithromycin) were used for comparison and absorbance (O.D) was determined at 420 nm by using spectrophotometer (Boyed, 1980). The minimum inhibitory concentration was calculated on the basis of lowest concentration of the extracts which inhibited the growth of bacteria after 24 hours of incubation period. The antifungal activity of *Carica papaya* extracts was estimated by using agar tube dilution method against four strains of fungus (*Aspergillus niger*, 0198; *Aspergillus flavus*, 0064; *Aspergillus fumigatus*, 66 and *Fusarium solani*, 0291) as per reported earlier through Ettebon and Nwafor (2009).

Brine shrimp assay

By following procedure reported by Ruch *et al.* (1989) cytotoxicity of plant extracts was determined by using brine shrimp lethality assays.

Table 1: Assessment of various phytochemicals from leaves and fruit extracts of *Carica papaya*.

Samples	Phytochemicals analyzed in samples						
	Alkaloids	Flavonoids	Polyphenols	Tannins	Cardiac glycosides	Saponins	Terpenes
Ethanolicleaves extracts	++	+	+	++	+	-	+
Ethanolicfruit extracts	+	+++	++	-	++	+	++

+, present; -, absent

Table 2: Assessment of Flavonoids and Phenolic contents of leaves and fruit extracts of *Carica papaya*.

Extracts	Total Flavonoids (mg rutin equivalent/g)	Total phenols (mg GAE/g)	Yield of extracts (%)
Ethanolic leaves extracts	47.16 ± 2.15 *	49.24 ± 2.16*	4.9 ± 0.7
Methanolic leaves extract	24.11 ± 0.51	26.66 ± 1.32	2.6 ± 0.4
n-hexane leaves extracts	15.17± 1.36	19.54± 1.71	2.5 ± 0.5
Ethanolicfruit extract	46.29± 1.23*	48.91 ± 1.32*	1.5 ± 0.6
Methanolic fruit extracts	22.15 ± 4.1	19.54 ± 2.93	1.9 ± 0.7
n-hexane fruit extracts	14.110 ± 0.51	16.66 ± 1.3	2.6± 0.4

Values are representing as mean +SD (n=3); *significantly higher value (p<0.05)

Table 3: Antioxidant potential of various extracts of *Carica papaya* at 100mg/ml

Extracts	DPPH	H ₂ O ₂	ABTS	FRAP assay	Ascorbic acid	Rutin
Leaves extracts						
Ethanol	0.114±0.01	2.132±0.05	1.323±0.08	0.135±0.01	1.214±0.81	1.772±1.83
Methanol	0.251±0.03	2.251± 0.04	2.252±0.07	0.154±0.01	1.252 ±0.34	2.424±0.84
n-hexane	0.311±0.01	2.653± 0.05	2.656±0.07	0.532±0.06	1.545 ±0.32	1.551±0.75
Chloroform	0.023±0.01	1.924±0.71	7.655± 0.15	0.163±0.01	1.825±0.45	1.662±0.52
Aqueous	3.081±0.01	8.132±0.26	9.134±0.26	0.184±0.05	1.751±0.52	1.874±0.35
Fruit extracts						
Ethanol	0.123±0.00	0.851±0.01	0.382±0.19	0.113±0.01	0.435±0.82	0.956±0.25
Methanol	0.254±0.03	2.352±0.01	2.252±0.07	0.135±0.01	1.225 ±0.34	1.434±0.83
n-hexane	0.125±0.01	1.193±0.81	1.911±0.52	0.196±0.05	1.362±0.55	1.125±0.35
Chloroform	0.223±0.01	1.254±0.93	1.653±0.74	0.091±0.06	1.554±0.36	1.435±0.54
Aqueous	0.318±0.01	1.435±0.75	1.864±0.43	0.182±0.01	1.635 ±0.72	2.254±0.36

concentration of 100µg/ml and IC₅₀ values (µg/ml) of radical scavenging 700 nm absorbance. Data represented in Means ± SD, (n = 3).

Table 4: Antibacterial activities of *Carica papaya* extracts in zone of inhibition in (mm).

Sample	Bacterial strains			
	<i>S. aureus</i>	<i>E. coli</i>	<i>K. pneumonia</i>	<i>B. subtilis</i>
Leaves extracts				
Ethanol	24.6±0.6	25.4±0.9	29.5±0.3	25.6±0.4
Methanol	21.6±0.8	22.6±0.6	26.6±0.7	24.6±0.6
n-hexane	17.2 ±0.5	17.3±0.8	17.6±0.4	16.5±0.7
Chloroform	18.3±0.6	19.2±0.3	14.2±0.4	15.8±0.5
Aqueous	12.4±0.8	15.6±0.6	11.3±0.5	11.6±0.3
Fruit extracts				
Ethanol	23.5±0.3	24.8±0.4	23.5±0.7	16.8±0.6
Methanol	22.6±0.9	23.5±0.7	22.6±0.8	13.4±0.5
n-hexane	19.6±0.5	19.2±0.9	19.2±0.6	14.5±0.5
Chloroform	13.4±0.4	15.7±0.8	21.6±0.5	15.7±0.9
Aqueous	11.5±0.7	13.2±0.7	13.5±0.4	11.2±0.7
Roxithromycin	24.3±0.9	22.6±0.7	12.3±0.9	13.6±0.8
Cefixime	13.5±0.3	11.6±0.5	11.4±0.8	12.7±0.9
DMSO	0.0	0.0	0.0	0.0

Data represented in Means ± SD, (n = 3)

Table 5: MIC ($\mu\text{g/ml}$) of *Carica papaya* extracts against various bacterial strains.

Extracts	Bacterial strains			
	<i>S. aureus</i>	<i>E. coli</i>	<i>K. pneumonia</i>	<i>B. subtilis</i>
Leaves extracts				
Ethanol	0.1 $\pm$ 0.6	1.2 $\pm$ 0.7	0.8 $\pm$ 0.5	1.4 $\pm$ 0.6
Methanol	0.5 $\pm$ 0.2	2.2 $\pm$ 0.3	1.1 $\pm$ 0.3	2.1 $\pm$ 0.4
n-hexane	1.7 $\pm$ 0.1	1.6 $\pm$ 0.9	0.7 $\pm$ 0.4	1.6 $\pm$ 0.7
Chloroform	1.8 $\pm$ 0.9	1.9 $\pm$ 0.5	1.2.2 $\pm$ 0.4	1.5 $\pm$ 0.5
Aqueous	2.9 $\pm$ 0.3	2.6 $\pm$ 0.7	2.7 $\pm$ 0.5	2.6 $\pm$ 0.3
Fruit extracts				
Ethanol	0.5 $\pm$ 0.6	0.8 $\pm$ 0.1	0.7 $\pm$ 0.9	1.1 $\pm$ 0.4
Methanol	0.8 $\pm$ 0.2	1.3 $\pm$ 0.4	1.1 $\pm$ 0.2	1.6 $\pm$ 0.6
n-hexane	1.6 $\pm$ 0.5	1.9 $\pm$ 0.8	1.9 $\pm$ 0.5	1.5 $\pm$ 0.5
Chloroform	1.4 $\pm$ 0.4	1.5 $\pm$ 0.9	1.6 $\pm$ 0.7	1.4 $\pm$ 0.6
Aqueous	1.5 $\pm$ 0.7	1.3 $\pm$ 0.7	1.8 $\pm$ 0.4	1.9 $\pm$ 0.3
Roxithromycin	1.3 $\pm$ 0.8	1.9 $\pm$ 0.5	1.2 $\pm$ 0.3	1.3 $\pm$ 0.5
Cefixime	1.5 $\pm$ 0.5	2.2 $\pm$ 0.6	1.1 $\pm$ 0.8	1.2 $\pm$ 0.5

Results are Means $\pm$ SD, (n = 3)**Table 6:** Antifungal activities of extracts of *Carica papaya*; Zone of inhibition in (mm)

Extracts	<i>Aspergillus niger</i>	<i>Fusariumsalani</i>	<i>Aspergillus flavous</i>	<i>Aspergillus fumigates</i>
Leaves extracts				
Ethanol	25.8 $\pm$ 0.5	24.8 $\pm$ 0.4	18.3 $\pm$ 0.3	21.5 $\pm$ 0.4
Methanol	23.4 $\pm$ 0.3	22.5 $\pm$ 0.7	16.5 $\pm$ 0.6	19.5 $\pm$ 0.2
n-hexane	18.3 $\pm$ 0.5	17.2 $\pm$ 0.5	17.8 $\pm$ 0.4	15.4 $\pm$ 0.8
Chloroform	16.3 $\pm$ 0.4	18.2 $\pm$ 0.3	16.3 $\pm$ 0.4	15.8 $\pm$ 0.5
Aqueous	11.4 $\pm$ 0.2	9.6 $\pm$ 0.3	11.6 $\pm$ 0.2	11.6 $\pm$ 0.3
Fruit extracts				
Ethanol	24.5 $\pm$ 0.1	19.8 $\pm$ 0.3	21.1 $\pm$ 0.5	19.6 $\pm$ 0.3
Methanol	22.6 $\pm$ 0.5	18.2 $\pm$ 0.7	19.3 $\pm$ 0.8	16.5 $\pm$ 0.5
n-hexane	18.6 $\pm$ 0.3	17.2 $\pm$ 0.9	17.2 $\pm$ 0.9	18.5 $\pm$ 0.6
Chloroform	16.4 $\pm$ 0.2	16.1 $\pm$ 0.9	16.6 $\pm$ 0.3	15.7 $\pm$ 0.9
Aqueous	10.5 $\pm$ 0.6	11.2 $\pm$ 0.4	11.5 $\pm$ 0.4	9.2 $\pm$ 0.5
Terbinafine	18.4 $\pm$ 0.3	16.3 $\pm$ 0.8	15.3 $\pm$ 0.5	14.6 $\pm$ 0.3

Results are Means $\pm$ SD, (n = 3).**Table 7:** Cytotoxicity screening of different concentration of *Carica papaya* extracts

Extracts	10 ($\mu\text{g/ml}$)	100 ($\mu\text{g/ml}$)	1000 ($\mu\text{g/ml}$)	LD50 ($\mu\text{g/ml}$)
Leaves extracts				
Ethanol	5.1 $\pm$ 0.6	12.1 $\pm$ 0.6	25.8 $\pm$ 0.3	<1000
Methanol	8.4 $\pm$ 0.7	14.5 $\pm$ 0.8	28.5 $\pm$ 0.7	800
n-hexane	34.6 $\pm$ 0.5	41.6 $\pm$ 0.5	49.7 $\pm$ 0.3	700
Chloroform	39.8 $\pm$ 0.3	46.9 $\pm$ 0.3	49.2 $\pm$ 1.4	100
Aqueous	47.4 $\pm$ 0.3	51.6 $\pm$ 0.7	59.7 $\pm$ 0.3	270
Fruit extracts				
Ethanol	6.5 $\pm$ 0.6	14.7 $\pm$ 0.1	24.3 $\pm$ 0.7	<1000
Methanol	7.3 $\pm$ 0.5	18.3 $\pm$ 0.4	26.5 $\pm$ 0.9	800
n-hexane	31.6 $\pm$ 0.5	36.9 $\pm$ 0.8	39.7 $\pm$ 0.5	700
Chloroform	33.4 $\pm$ 0.5	36.5 $\pm$ 0.9	39.1 $\pm$ 0.3	100
Aqueous	51.5 $\pm$ 0.7	54.3 $\pm$ 0.7	56.3 $\pm$ 0.4	260

Values are Mean $\pm$ SD, (n=3) and significantly different (P<0.05); positive control: saline sea salt.

STATISTICAL ANALYSIS

All experiments were done in replicates and values were represented as means $\pm$ SD as reported by Steel and Torrie (1980).

RESULTS

Phytochemical analysis is prerequisite for investigation of pharmacological potential of plant extracts and its fractions. According to results obtained in this study alkaloids, flavonoids, phenols, tannins, cardiac glycosides, saponins and terpenes were found in fruit and leaves extracts of *Carica papaya* (table 1). Quantification of bioactive compounds like phenolic and flavonoids from fruit and leaves extracts were carried out (table 2). It was observed that ethanolic leaves extracts of *Carica papaya* contained higher amount of total phenols (49.24 ± 2.16 mg GAE equivalent/g) as well as flavonoids (47.16 ± 2.15 mg Rutin equivalent/g) as compared to all other extracts analyzed (table 2).

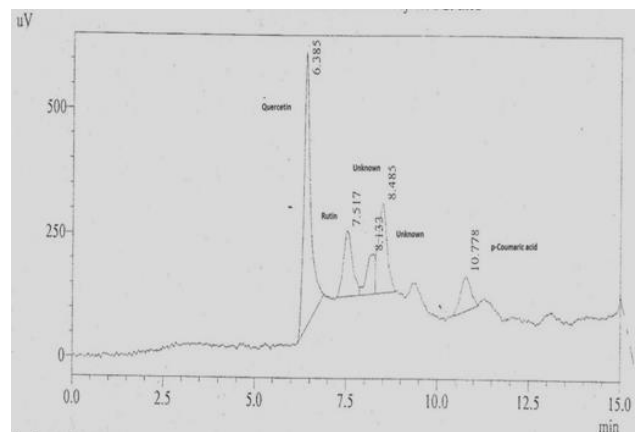


Fig. 1: HPLC analysis of ethanolic fruit extracts of *Carica papaya*

Analysis of various extracts of *Carica papaya* with HPLC revealed that higher quantity of quercetin was present in ethanolic leaves extracts as compared to ethanolic fruit extracts. Canini *et al.* (2007) found quercetin in *Carica papaya* samples but concentration reported by them were lower as compared to quantity of quercetin found in current study (figs. 1 and 2).

To check the antioxidant potential of leaves and fruit extracts of *Carica papaya*, five different assays i.e. DPPH, H_2O_2 , ABTS phosphor-molybdate and reducing power assays were performed and values obtained were compared with ascorbic acid and Rutin used as standard in this experiment. Although all solvents extracts have shown a significant antioxidant potential, but antioxidant potential shown by ethanolic leaves and fruit extracts was significantly higher than other solvent extracts. However, in some cases the values were lower than positive control (ascorbic acid) and standard rutin (table 3).

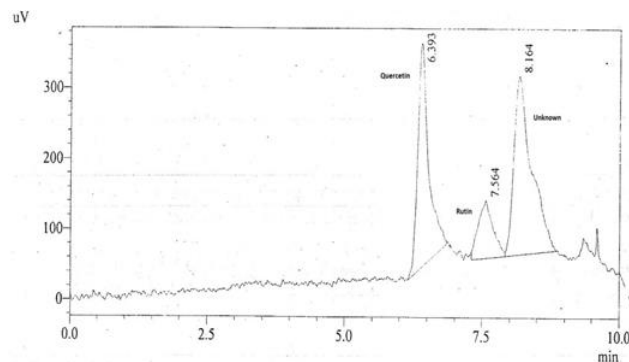


Fig. 2: HPLC analysis of ethanolic leaves extracts of *Carica papaya*

The ethanolic extracts of leaves and fruit extracts have been found to possess active inhibitory potential against *S. aureus*, *E. coli*, *K. pneumonia* and *B. subtilis* strains as compared to all other extracts, cefixime and DMSO, however, lower zones of inhibition were observed as compared to roxithromycin (standard) (table 4). Minimum inhibitory concentration indicates significant antimicrobial potential of extracts and data obtained, through the determination of MIC of various extracts and antibiotics are presented in table 5.

Results in table 6 represented the antifungal activity of plants extracts, showed significant higher antifungal activity of ethanolic leaves extracts (25.8 ± 0.5 mm) followed by ethanolic fruit extracts (24.5 ± 0.1 mm) and methanolic leaves extracts (23.4 ± 0.3). However, lowest activity was shown by aqueous leaves extract (10.5 ± 0.6 mm). Extracts prepared in organic solvents have shown reliable antifungal activities and significantly comparable to already reported by Fawole *et al.* (2008) and Parekh and Chanda, (2007), in which water extracts showed significantly less fungal toxicity than organic solvents, as indicated in present study as well (table 6).

Three different dilutions of *Carica papaya* leaves and fruit extracts (10, 100 and 1000 μ g/ml) were prepared to check brine shrimp's cytotoxicity assay. The results revealed parricidal potential of extracts, however, concentration of extracts was directly proportion to degree of lethality (table 7). It was assumed that plant extracts might possess antitumor components in the form of essential phytonutrients. The plant extracts whose value are i.e. $LD_{50} < 1000 \mu$ g/ml was biologically active while $LD_{50} > 1000 \mu$ g/ml was biologically inactive (non-toxic) (table 7).

DISCUSSION

Different plant based phytochemicals possess active bioactive potential and widely studied against different ailments. Based on traditional knowledge about use of *Carica papaya*, the current study was designed to provide

scientific proof about safe and beneficial consumption of leaves and fruit of this plant. In current study the different leaves and fruit ethanolic extracts found to have higher amount of total phenol and flavonoids contents as compared to other extracts analyzed (table 2, figs. 1 and 2) indicated potential of leaves and fruit of *Carica papaya* and suggested its use for human health. The results of phytonutrients obtained in present study were comparable with results reported earlier by other authors including Kim *et al.* (2003). Phenolic compounds are secondary metabolites naturally present in all plants in wider range, possess free radical scavenging activity and considered as potential antioxidant agents having great impact on human health (Jayaprakash *et al.*, 2001). Phenolic compounds are very important antioxidants, having various application like reducing agents, hydrogen donors, and free radical scavengers, quenchers of oxygen and as cell saviors. The concentration level of flavonoids found in *Carica papaya* during our study was higher than reported earlier by Omotade *et al.* (2011). Flavonoids possess antioxidants, antiviral, anti-fungal and antibacterial activities but also protect liver and stomach from different disorders (Okeniyi *et al.*, 2007). Quercetin is a flavonoids found in leaves and fruit extracts of *Carica papaya* (table 2, figs. 1 and 2) prevents human body from releasing histamines that cause an allergic response in the body. Quercetin also prevents plaque buildup in arteries (atherosclerosis) that can lead to heart attack, stroke, and obesity (Chirumbolo, 2012). It was reported by Aqil *et al.* (2006) that plant extracts containing isoflavones, flavonoids, anthocyanin, coumarinlignans, catechins and isocatechins always have good potential of antioxidant activities.

Analysis of *Carica papaya* extracts with HPLC revealed the presence of reliable quantity of quercetin (figs. 1 and 2) and probably this flavonoid along with other secondary metabolites was responsible for majority of biological activities of these extracts as reported by Rathee *et al.* (2008). Whereas Devasagayam *et al.* (2004) found that drugs having good potential of antioxidants are useful for the treatments of complex infections of human population like atherosclerosis, stroke, diabetes, Alzheimer's disease and cancer etc.

All extracts showed a significant antibacterial potential against both gram positive and gram negative bacterial strains as well as fungal strains which indicates that plants extracts composed of antimicrobial components such as flavonoids etc. that can be used to treat infectious disorders caused by the severe resistant pathogenic microorganisms. The current findings support the results reported by other authors with slight variations (Ettebong, and Nwafor, 2009). The use of plant based drugs against infectious diseases around the world have long history, that have strong potential for effective treatments of antibiotic-resistant infections, which is larger public

concern and increasing globally (Fawole *et al.*, 2009; Parekh and Chanda, 2009). The results obtained in current study disclosed instability in the inhibitory concentrations of each extract for given bacteria. The lowest MIC was observed for ethanol extracts might be due to its purity or solubility of plant materials in relevant solvents (table 5). Results found in present study were comparable to results reported by other authors like Guessan *et al.* (2007).

Results of brine shrimp lethality obtained in current study were comparable with results reported by Sandeep *et al.* (2009). The brine shrimp assay provides important information about bioactivity of any plant extract that might be correlated reasonably with cytotoxic and antitumor properties. This assay is a practically an important tool for preliminary assessment of toxicity and it has been used for the detection of fungal toxins, toxicity of plant extracts, heavy metals, and cytotoxicity testing of dental materials. The LC₅₀ value <1000 µg/mL are consider significant for crude extract (Hossan *et al.*, 2009). The lethality of the extract increased with concentration suggesting that extracts may be consist of some lead compounds with antitumor properties which need further study to understand their complete phytochemistry.

It is concluded that the *Carica papaya* leaves and fruit extracts contained valuable bioactive secondary metabolites (Polyphenols and Flavonoids). These extracts have shown good potential to scavenge free radicals, inhibited the growth of pathogenic bacterial and fungal strains as well as provided lower cytotoxicity levels during brine shrimps assays. It is predicted that, a use of appropriate doses of leaves and fruit extracts of *Carica papaya* is helpful to improve many human disorders especially when antibiotics resistance or reduction in platelet levels in blood of any individual is in question. These pharmacological properties have made papaya fruit and leaves suitable for human consumption to minimize many of human ailments. Further research is needed to isolate lead compound that might be required by industries for preparation of drugs to cure various liver ailments.

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