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EFFECTS OF CARICA PAPAYA ON THE PREVENTION OF FUNCTIONAL DYSPEPSIA

[1]Dr. Muneeb Altaf, [2]Dr. Zunaira shafiq, [3]Dr. Sania Saleem
[1]Medical Officer, PKLI Hospital Bedian Road Lahore
[2]THQ Harronabad
[3]King Edward Medical University

Abstract:
***Objective**: A set of chronic or reverting dyspeptic signs in the nonexistence of structural organic lesions is known as Functional dyspepsia (FD). About 15-20% general population of advanced countries and 14-22 % of Pakistan undergoes through FD. The purpose of this study is to assess the efficacy of Carica papaya extract (CP) in avoiding FD in human volunteers.*
***Methodology**: A communal, randomized, placebo-controlled, multi-centred and double-blind clinical trial conducted over the systematic random specimen. After taking written consent of 200 diagnosed FD cases inducted and randomly and equally assigned CP extract or placebo treatment groups. Observed 7 days' pre-trial non-medication period. Six weeks of treatment received by all patients. Gastrointestinal symptom score (GIS) development was the prime variable result comprising 10 dyspeptic symptoms rated evaluation on a Likert scale. At starting of trial and subsequently after 2, 4- and 6-weeks dyspeptic symptoms were evaluated.*
***Results**: In this study 200 patients fully participated for trial (age 36.31±9.711 years, 60% female). Clinically substantial improvement presented by CP group as compared to placebo. Within initial 2 weeks in CP group, the GIS considerably reduced as compared with placebo (p0.05). In the second- and third-week timeframe signs improved more in CP group ($p < 0.05$) and after 6 weeks, 3.1% on placebo treatment and 95.7% on CP were fully relieved of FD (p0.001).**Conclusions**: As equalled with placebo, CP extract was expressively active gastro-protective.*
Keywords: *Bloating, Belching, Dyspepsia, Placebo, Gastro-Protective, Epigastric Zone*

Corresponding Author:
Dr. Muneeb Altaf,
Medical Officer,
PKLI Hospital Bedian Road Lahore

QR code

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INTRODUCTION:

Dyspepsia denotes a variety of indications contained in the epigastric zone. Indigestion general signs comprise early satiation, postprandial plumpness, epigastric burning and epigastric ache whereas sometimes abdominal bloating or belching and nausea ensues. The existence of dyspeptic symptoms in non-availability of an organic reason is described as FD [1]. Functional gastrointestinal disorders (FGIDs) are widespread and victimized people having deprived way of life. The analysis of FGIDs has generally depended on the usage of self-report inquiry as structural abnormalities are subtle due to which these disorders are different from other gastrointestinal (GI) disorders. The Rome criteria classify and diagnose FGIDs. No proof of physical or organic syndrome for the previous three months with the inception of indication 6 months earlier of conclusion [4, 5]. The standards reformed with the development of scientific facts. With the release of Rome IV, criteria amended in May 2016. Post-prandial fullness as well as early satiation, epigastric burning and bothersome epigastric pain are taken into attention out of major FD's symptoms [6, 7].

People-based research on factual FD is rare because of complications in excluding physical illness in more people. Depending on geographical location, the uninvestigated dyspepsia (UD) varied among 7%-45%, whereas the presence of FD ranged from 11% to 29.2% [8]. In one more report, the presence of FD varied among 5-11 percent worldwide [9, 10] and 8%-23% in Asia [11]. In the West part of Iran, the popularity of dyspepsia was 54.6% [12] and in India reported to be 30.4% [13]. Yet so communal in Pakistan, precise information is not existing till now. In Pakistan, FD involved 11-15% of a physician's practice [14]. FD existence ranging 14-22% invariant researches in Pakistan [15]. FD found in 76% of patients with dyspepsia [16]. Dyspepsia considered ideologically in 50 % patients as no definite reason noted. Dyspepsia's assessment consists of detailed background and physical investigation, with importance imparted to the signs which can cause the existence of the critical illness. The very common harmful reasons for stomach include hurry, worry and curry which are very common in Pakistan.

In the treatment of human diseases, plants role may not be overlooked. Plants are in use since long as modern drug therapy source [17]. Customarily, plants are in use for the preparation of around 25% of recent drugs. Almost 80% of the African people used customary medication for communal diseases and basic health upkeep. About 50% people of Europe, North America, 70% Canadians and 90% Germans people are using traditional medicines. As per the World Health Organization (WHO), about 80% population of the world depends upon traditional medicine [18]. Papaya efficiently enhanced every kind of digestive and abdominal ailments and prescribe as a cure for hyperacidity and dyspepsia [19]. The anti-ulcerogenic action of an aqueous excerpt of Carica papaya fruit noted in aspirin - persuaded ulcer in rats [20] and likewise, it confirmed on an indomethacin-made peptic ulcer in male albino rats [21].

Extracts of the variants study on the efficacy of Carica papaya (CP) are as under: -

a. CP leave's ethanol excerpt afforded safeguard in rats for aspirin-induced gastric ulcer [22].
b. CP's Gastroprotective effect discovered by R Gadekar, et al on rats [23]
c. Anti-ulcer activity of CP seed extracts showed in rat's ulcers induced indomethacin [24].
d. In the gastritis treatment, the efficacy of CP fruit documented [25].
e. Aqueous excerpt of fresh CP ovary examined for mucus secretion, anti-ulcer, pepsin binding effects and anti-acid secretory in rats for indomethacin-induced ulcers found that extract had positive effects [26]
f. In humans, papaya readiness subsidized to the upkeep of digestive region functioning [27].

MATERIAL AND METHODS:

CP excerpt arranged through fresh papaya fruit, one kg produced 500 grams in most pulp and after dryness, pulp generates 50 gm powder. The micro-prevention method uses for gaining excerpt, 200 grams' powder treated over anaerobic transferal causing into 20 gm deposit which further gets through ethanolic-aqueous removal, Final extract than mixed into water to produce 0.2 ppm mixture (1 microgram extract in 5 ml). Five millilitres orally placebo was given to normal group and post-meal (6 weeks), orally 5 ml CP excerpt diluted in 100 ml of water thrice a day was given to involving the group. Smell, colour, dose and taste of placebo and CP extract were matching.

In the city of Multan, a randomized, double-blind, multicenter, placebo-controlled trial conducted through random specimen for 6 weeks with the help of erratically chosen best family doctor working in that community. Hence, chosen ten of fifty family doctors partaken the study. Following formula use for assessment of sample size:

$ne= nc=[(Z_{a/}+ZP)2\&2(\backslash+l)/X)/(Mc\text{-}ue)^2$

The ratio (X) of C (papaya group to placebo group) was 1:1 and power of 80% (1 - *X)* at 5% (X) of importance level, the trial extent of o*ne* = *NC* = 100 patients per group taken. The total sample size was 200 because of the control group.

Keeping in view care and moral use, CP excerpt has been widely recycled in a number of studies particularly for increasing the platelet count in patients of dengue [28]. Those FD patients are chosen who were attending family physicians at their clinics and after taking written approval for involvement in the trial. Use the Rome III criteria for the inclusion of the patients and FD cases with satisfying one or more of the following symptoms included in the trial.

a. Post-prandial fullness (nasty feeling like long food perseverance in the stomach)
b. Early satiation (sensation of congestion of stomach even with low food)
c. Epigastric pain,
d. Epigastric burning (feeling of heat)

Post selection, all patients clarified regarding usage of medicine. Period of the trial was six weeks and after administration, effectiveness evaluated at week 2, 4 and 6. After 7 days, the patients administer into 6 weeks' placebo or CP extract treatment. As an incentive, these patients were given a free supply of extract and lab tests. Those patients who were not satisfying Rome III criteria or having diseases (chronic irritable bowel syndrome, and heart, lung, liver, kidney, intestinal or extra-intestinal, allergy, drug abuse) was not registered for a trial. Moreover, the following were also exclude from the trial:

a. Participants in any other clinical trial in previous 3 months.
b. Surgically operated in previous 6 months.
c. Severe organic or psychiatric illness
d. Chronic malabsorption
e. Pregnant and lactating mothers
f. Patients using any antibiotic, bismuth salt, a proton-pump inhibitor, prokinetic agents and drugs with an anti-kinetic action.
g. Patients using any other herbal medicines.
h. Who have complaints of black stool or abrupt weight loss?
i. Unwilling patients

If the chosen patient failed to fulfil the requisite conditions, then the following patient satisfying the criteria was chosen. They put FD patients in the control group or CP group as per the decided order in such a way so equal participants inducted into control and CP groups. Because of the double-blinded study, neither researchers nor patients were known about the placebo and actual extract as both the samples were of same colours and supplied in same looking bottles. Bottles were marked simply with code numbers.

Data collected and compiled at all over the trial period. At the beginning, demographic features of study population noted. Frequency table prepared and means and standards calculated for demographic profile. (Table 1).

With the GIS system, evaluation of FD symptoms was making, which assess the severity of 10 FD's symptoms. Symptoms based assessment of FD Patients was made with the usage of following Likert scale:

a. No problem
b. Minimal (ignorable without effort).
c. Mild (ignorable with effort).
d. Moderate (Not ignorable but not affecting daily life activities).
e. Moderately severe (cannot be ignored and occasionally limits my daily activities).
f. Severe (Not ignorable but limiting daily life activities).
g. Very severe (Not ignorable and noticeably limiting daily life activities and sometimes requires rest).

Pre and post intervention, routine lab examinations (lipid profile, serum albumin, CBC, total protein and renal profile) conducted in CP group. The efficiency of CP extract and placebo evaluated by Gastrointestinal Symptom (GIS) scale after 2, 4 weeks and at the end of the trial. Information gathered, collected and investigated over SPSS21. Paired t-test was applied for assessment of blood parameters for efficient results at baseline on GIS Scale (Table 2 and 3). For CP and control group's differences at the start and beyond 6 weeks, sample t-test was applied (Table 4).

RESULTS:

All the 200 FD patients were adults and 60 percent of the patients were female (Table 1). Patients were not having any noticeable variance in a start in FD symptoms, however, major development observed ($p<0.0001$) after 2 weeks' trial in the CP group with a small progress in the control group. FD signs further progressed after 4 weeks in CP group ($p<0.0001$) but decline noticed in the control group. Post 6 weeks trials, noteworthy development (p-value<0.0001) seen in CP group (Table 3).

After 6 weeks in CP group substantial variance ($p<0.01$) noticed in all indications with respect to the

Placebo group, where no development was found (p>0.05). (Table 4).

Table – I: Gender Distribution

Gender	Number	Percentage
Male	80	40
Females	120	60

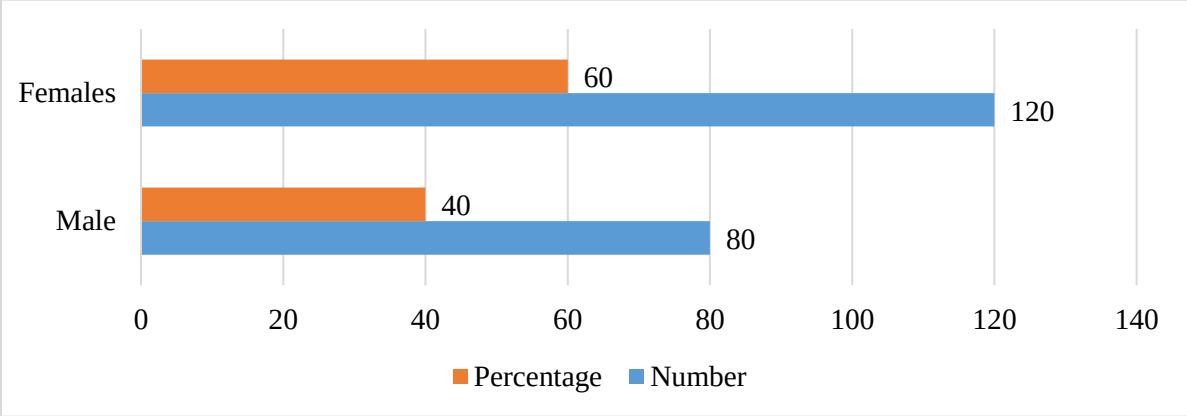


Table – II: Demographic Profile

Parameter	Mean/ Min Limit	±SD/ Max Limit
Age	36.31	9.71
Age Limit	18	55

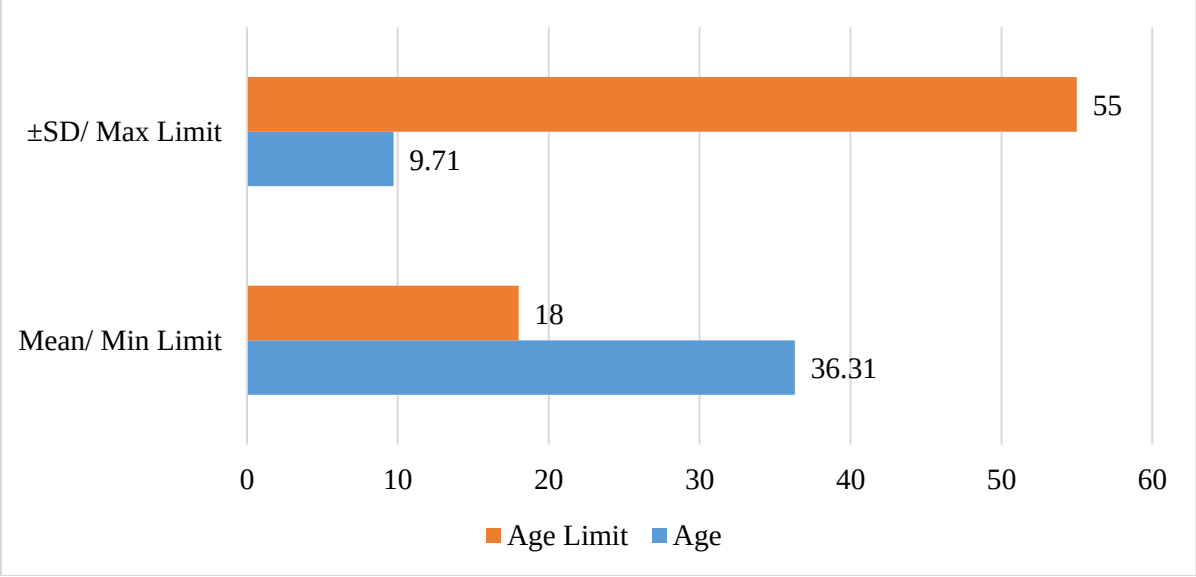


Table – III: Blood Parameter Analysis Before and After Intervention

Parameter	At Baseline		After Six Weeks		P-Value
	Mean	±SD	Mean	±SD	
Hb	13.26	1.47	13.51	1.49	> 0.05
Polymorphs	60.53	1.98	59.42	1.77	
Lymphocytes	33.45	1.64	32.12	1.48	
Monocytes	3.16	1.47	2.87	1.34	
Eosinophils	2.87	0.84	2.77	0.81	
BSR	116.07	17.51	131.87	17.51	
Bilirubin	0.575	0.2	0.612	0.22	
Alanine Transaminase	27.45	8.03	26.32	7.87	
Alkaline Trans phosphatase	29.89	7.64	27.76	7.32	
Alkaline Phosphatase	121.67	14.13	124.82	15.23	
Blood Urea	25.49	12.89	23.31	11.54	
Serum Creatinine	0.719	0.08	0.673	0.06	
Serum Cholesterol	163.44	9.49	165.28	10.21	
Serum Triglycerides	149.53	16.1	153.65	16.34	
High Density Lipoprotein	43.95	6.15	41.12	5.87	
Low Density Lipoprotein	136.16	11.4	141.78	12.91	
TLC	7909	1900	8120	1967	
Platelets	252710	42887	255860	41650	

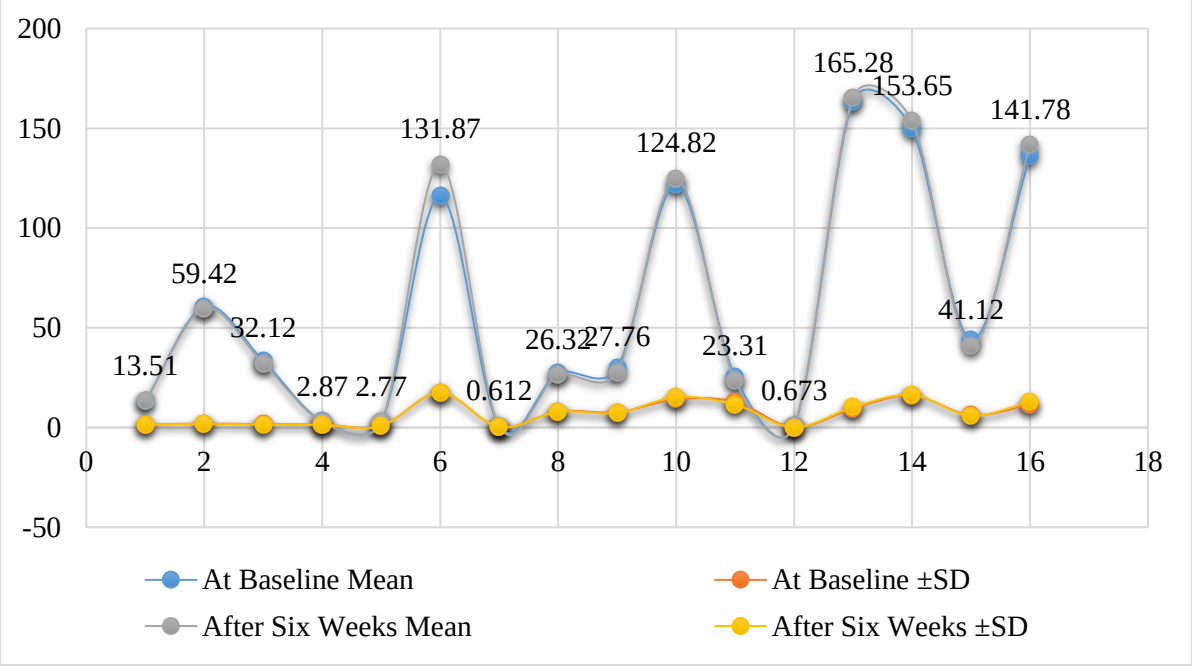


Table – IV: Efficacy Outcomes at various time intervals

Symptoms		Epigastric Pain	Nausea	Vomiting	Postprandial Fullness	Early Satiation	Heart Burn	Regurgitation	Epigastric Burning	Belching	Bloating
Baseline	CP Extract	6.80	6.20	4.50	5.90	5.40	6.30	5.80	6.90	6.70	5.90
	Placebo	6.80	6.20	4.50	5.90	5.40	6.30	5.80	6.90	6.70	5.90
After Two Weeks	CP Extract	0.60	0.90	1.20	1.40	1.10	0.30	0.80	0.60	0.80	0.90
	Placebo	3.70	4.30	2.10	4.20	4.30	4.60	4.90	3.50	4.20	4.80
	Difference	<0.05									
After Four Weeks	CP Extract	0.20	0.10	0.00	1.20	0.60	0.00	0.20	0.00	0.20	0.20
	Placebo	3.80	4.60	2.30	4.40	4.70	5.10	5.00	4.10	4.70	5.10
	Difference	<0.05									
After Six Weeks	CP Extract	0.00	0.00	0.00	0.20	0.00	0.00	0.00	0.00	0.00	0.00
	Placebo	4.90	4.60	2.10	5.30	4.90	5.40	5.30	5.40	4.90	5.80
	Difference	<0.05									

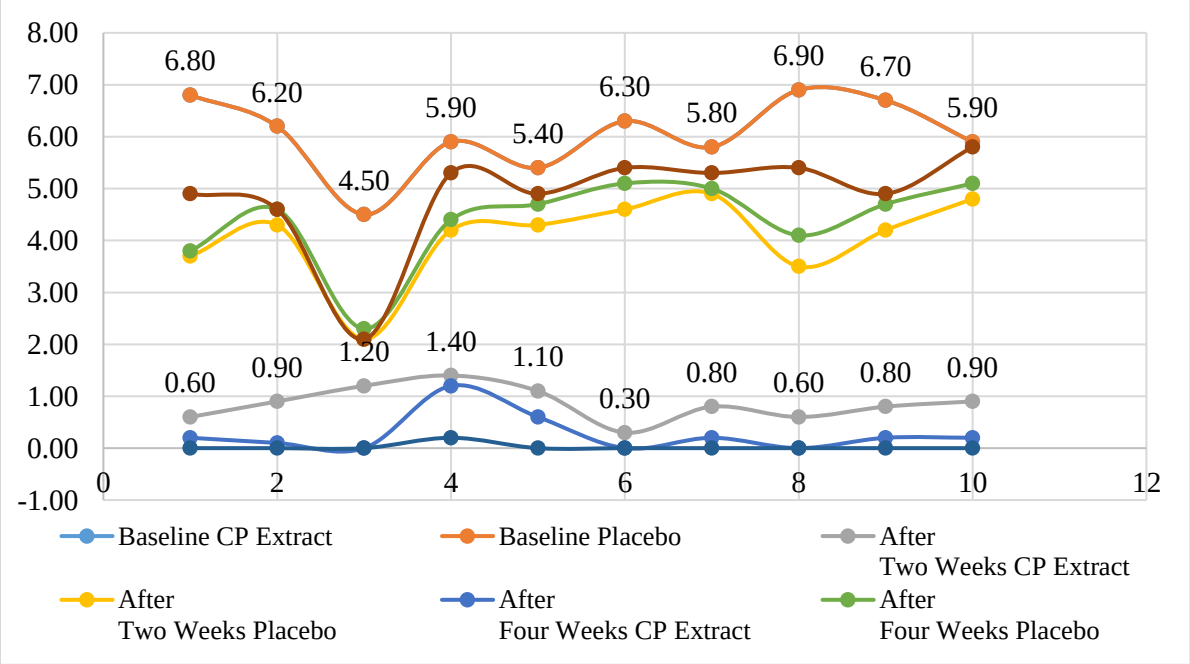
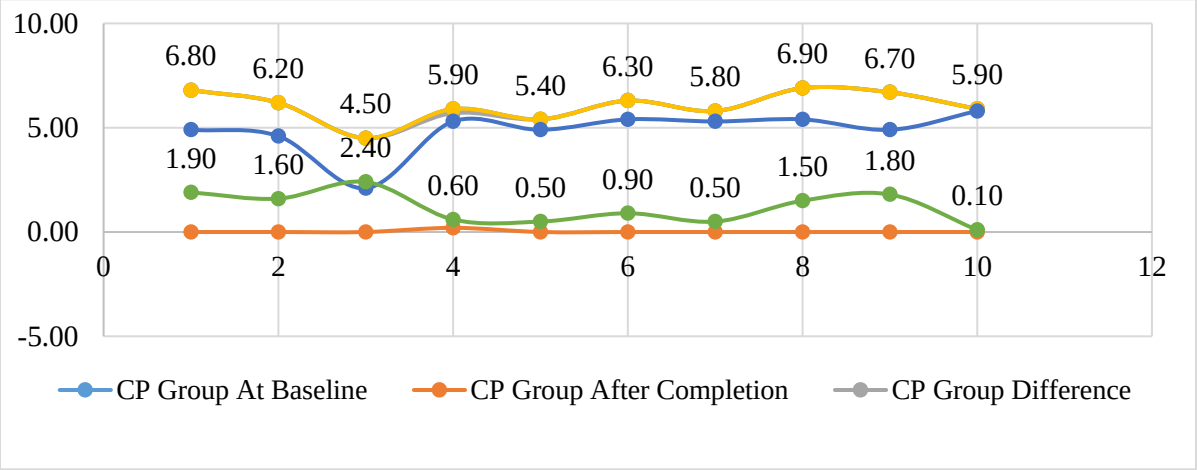


Table – V: Experimental and Control Group Outcomes with Differences

Symptoms		Epigastric Pain	Nausea	Vomiting	Postprandial Fullness	Early Satiation	Heart Burn	Regurgitation	Epigastric Burning	Belching	Bloating
CP Group	At Baseline	6.80	6.20	4.50	5.90	5.40	6.30	5.80	6.90	6.70	5.90
	After Completion	0.00	0.00	0.00	0.20	0.00	0.00	0.00	0.00	0.00	0.00
	Difference	6.80	6.20	4.50	5.70	5.40	6.30	5.80	6.90	6.70	5.90
	P-Value	< 0.01									
Placebo Group	At Baseline	6.80	6.20	4.50	5.90	5.40	6.30	5.80	6.90	6.70	5.90
	After Completion	4.90	4.60	2.10	5.30	4.90	5.40	5.30	5.40	4.90	5.80
	Difference	1.90	1.60	2.40	0.60	0.50	0.90	0.50	1.50	1.80	0.10
	P-Value	> 0.05									



DISCUSSION:

Functional dyspepsia (non-ulcer) is a vastly common ailment [8, 9, 10]. Perpetual treatment for most patients does not exist due to numerous causes like anxieties, bad routine, food habits and many more reasons [11, 12]. There have been several efforts to practice herbal measures, vegetables and fruits to form the irritation appearance of FD and some of them verified somewhat productive [13]. In this study, efforts were planted into innovation of cure for FD which should have the immediate and harmless result, cost-effective, minor dose and having a strong caring role.

This research is exclusive in numerous features. CP extract was consumed in very small quantity, moreover, its prompt results in freeing FD symptoms not underlined in preceding researches. Micro-prevention technique used for the first time to prepare the ex-tract and ethanolic-aqueous extract was also manipulated in humans for the first time to control FD. Furthermore, it invites further studies for human health on more parts of CP as roots, leaves and flowers.

The outcomes of CP extract assessed and connected with placebo and come across that in this experiment, with a comparison to placebo sizable progress was a witness in the CP extract group.

With comparison to existing medications in use for FD handling, CP extract was exceptional for unscented, colourless, no adverse results, arranged locally and inexpensive. The therapy resulted significantly well. Widespread assessments would entail assessing the efficiency of CP extract.

As a result, it was apparent that in releasing the

indications of FD, CP abstract was more efficient with respect to placebo. Yet, for determining the effectiveness of CP extract, follow up experiments would be required.

CONCLUSION:

Recently, FD develops as a communal ailment because of the poor quality of life. Papaya is having a better impression for FD treatment. Our study makes a new addition to the previous researches because for the first time in humans CP extract was studied. As compared to placebo the result of CP extract in the reduction of FD was noticeably greater as all patients on CP treatment and a few on placebo fully relieved from FD after 6 weeks. During this trial, as compared to the placebo group, side effects were almost nil in the CP group. It would be a worthy adding into remedies archive for FD and categorized by ordinary, natural, quick relief, micro dose, tasteless, cost-effective, and having no adverse effects after lengthy use.

REFERENCES:

1. Tack J, Talley NJ. Functional dyspepsia--symptoms, definitions and validity of the Rome III criteria. Nat Rev Gastroenterol Hepatol. 2013Mar;10(3):134-41. https://doi.org/10.1038/nrgastro.2013.14
2. Mearin F, Calleja JL. Defining functional dyspepsia. Rev Esp Enferm Dig. 2011Dec;103(12):640-647. https://doi.org/10.4321/S1130-01082011001200006
3. Wang X, Luscombe GM1, Boyd C, Kellow J, Abraham S. Functional gastrointestinal disorders in eating disorder patients: altered distribution and predictors using ROME III compared to ROME II criteria. World J Gastroenterol. 2014Nov 21;20(43):16293-9 https://doi.org/10.3748/wjg.v20.i43.16293
4. Alexander C. Ford. Premysl Bercik, David G. Morgan, CarolinaBolino, Maria Ines Pintos-Sanchez, Paul Moayyedi. The Rome III Criteria for theDiagnosis of Functional Dyspepsia in Secondary Care Are Not Superior to Previous Definitions. Gastroenterology. April 2014.146(4):932-940
5. Alexander C. Ford, Premysl Bercik, David G. Morgan, Carolina Bolino, Maria Ines Pintos–Sanchez, Paul Moayyedi. Validation of the Rome III Criteria for the Diagnosis of Irritable Bowel Syndrome in Secondary Care. Gastroenterology.Volume145, Issue 6, December 2013, Pages 1262-1270.
6. Max J Schmulson, Douglas A Drossman. What Is New in Rome IV. J Neuro gastroenterol Motil. 2017 Apr; 23(2): 151–163. https://doi.org/10.5056/jnm16214
7. Hidekazu Suzuki. The Application of the Rome IV Criteria to Functional Esophagogastro duodenal Disorders in Asia. J Neuro gastroenterol Motil. 2017 Jul; 23(3): 325–333. https://doi.org/10.5056/jnm17018
8. Mahadeva S, Goh KL. Epidemiology of functional dyspepsia: a global perspective. World J Gastroenterol.2006 May 7;12(17):2661-6. https://doi.org/10.3748/wjg.v12.i17.2661
9. Ford AC, Marwaha A, Sood R, Moayyedi P. Global prevalence of, and risk factors for, uninvestigated dyspepsia: a meta-analysis. Gut 2015; 64:1049. https://doi.org/10.1136/gutjnl-2014-307843
10. Talley NJ, Ford AC. Functional Dyspepsia. N Engl J Med 2015; 373:1853-1863 https://doi.org/10.1056/NEJMra1501505
11. Uday C Ghoshal,1 Rajan Singh. Epidemiology of Uninvestigated and Functional Dyspepsia in Asia: Facts and Fiction. J Neuro gastroenterol Motil. 2011 Jul; 17(3): 235–244. https://doi.org/10.5056/jnm.2011.17.3.235
12. Vahid Yousefinejad, Ebrahim Ghaderi, Dyspepsia prevalence in general population aged over 20 in the west part of Iran, JPMA july 2012. http://jpma.org.pk/full_article_text.php?article_id=3550
13. Kumar A, Pate J, Sawant P. Epidemiology of functional dyspepsia. J Assoc Physicians India. 2012Mar;60 Suppl:9-12.
14. Azam. Z**.** Functional GI disorders include Functional Dyspepsia and Irritable Bowel Syndrome. World Digestive Health Day Meetings at DUHS, SIUT. Pulse International. May 29th 2015. http://www.pulsepakistan.com/index.php/main-newsjuly-1-15/1237-functional-gi-disorders-include-functional-dyspepsia-and-irritable-bowel-syndrome-dr-zahid-azam
15. Khar HB, Umar M, Khurram M, Khan M, Mohammad Z, Goraya F, et al. Endoscopic and histopathological evaluation of 306 dyspeptic patients. Pak J Gastroenterol 2003; 17: 4-7.
16. Anwar.S.O, Ambreen. S, Ashraf. H.M. Frequencyof peptic ulcer disease in patients of dyspepsia an analysis of upper gastrointestinal endoscopy. PAFMJ. March.2010 Vol 60(1)
17. Biljana Bauer Petrovska. Historical review of medic implants usage. Pharmacogn Rev. 2012 Jan-Jun; 6(11): 1–5. https://doi.org/10.4103/0973-7847.95849
18. WHO traditional medicine strategy: 2014-2023.http://www.who.int/medicines/publications/traditional/trm_strategy14_23/en/

19. Aravind. G, Debjit Bhowmik, Duraivel. S, Harish. G. Traditional and Medicinal Uses of Carica papaya. Journal of Medicinal Plants Studies. 2013. Vol. 1(1) 173. http://www.springerlink.com/content/qp4135t8v0j08048/fulltext.pdf
20. Ologundudu, A. O. Lawal, I. A. Ololade, A. A. Omonkhua & F. O. Obi: The Anti-ulcerogenic Activity of Aqueous Extract of Carica Papaya Fruit on Aspirin – Induced Ulcer In Rats. TheInternet Journal of Toxicology. 2008 Volume 5.
21. Oloyede HO, Adaja MC, Ajiboye TO, Salawu MO. Anti-ulcerogenic activity of aqueous extract of Carica papaya seed on indomethacin-induced peptic ulcer in male albino rats. J Integr Med.2015 Mar;13(2):105-14 https://doi.org/10.1016/S2095-4964(15)60160-1
22. Christian E. Odo and Agatha I. Odo. Ethanol extract of the leaves of Carica papaya affords protection against aspirin-induced gastric ulcer in rats. Journal of Pharmacy Research 2017Vol.11(8):1025-29
23. R Gadekar, PK Singour, PK Chaurasiya, RS Pawar, UK Patil. Potential of some medicinal plants as an antiulcer agents Pharmacogn Rev. 2010 Jul-Dec; 4(8): 136–146. https://doi.org/10.4103/0973-7847.70906
24. Gadzama P. A, Wurochekke A. U, Mahmoud, S.J. Anti-Oxidant Activity of Carica Papaya Seed Extracts on Indomethacin-Induced Ulcer in Rats. IJSR,2016 Vol 5(1):699-703 https://doi.org/10.21275/v5i1.NOV152843
25. David J Simbo. An ethnobotanical survey of medic inalplants in Babungo, Northwest Region, Cameroon. J Ethnobiol Ethnomed. 2010; 6:8. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2843657/ https://doi.org/10.1186/1746-4269-6-8
26. Bamidele V. Owoyele, Atinuke F. Gbago and Olabode S. Ashaolu. Gastroprotective effects of aqueous extract of unripe carica papaya fruit in rats. pjms, 2013 Vol.11(2):1-11
27. Muss. C, Mosgoeller. W, Endler. T. Papaya preparation (Caricol ®) in digestive disorders. Biogenic Amines 2012 Vol. 26(1):1-17
28. Jaykaran Charan, Deepak Saxena, Jagdish Prasad Goyal, Sandul Yasobant. Efficacy and safety of Carica papaya leaf extract in the dengue: A systematic review and meta-analysis. Int J Appl Basic Med Res. 2016 Oct-Dec; 6(4): 249–254. https://doi.org/10.4103/2229-516X.192596