



Efficacy of Pylorin (poly herbal formulation) for the management non Ulcer condition of stomach and *H. Pylori* limited Dyspepsia

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Abstract

More than half of the world population present with the varying degree of dyspeptic situation in gastroenterology setting in health care system, available options of medications has not shown long term control over the ailment if there is, after some time relapse of the disease. In current era need for the development of alternate option to relief dyspepsia symptom has got much importance, dyspepsia affects more than 50% of the world population in majority of the cases it is not associated with identifiable lesion like *H. pylori* infection otherwise it's eradication may spontaneously relieve this ailment. This study was carried out for the assessment of the efficacy of the poly herbal formulation Pylorin for the management of dyspepsia in non-ulcer cases. Study was randomized single blind multicenter parallel arm study, carried at Shafa ul Mulk Memorial Hospital for Eastern Medicine, Hamdard University Karachi. All the process of Pylorin preparation was carried out at Hamdard University Karachi. Overall 670 total participants were enrolled in the study, 330 patients who receive Pylorin comprise 138 female and 192 male. 264(80%) patients got complete relief, 49(15%) patients report only mild relief in their symptom while 17(5%) cases show no improvement. While in case of placebo only 27 cases shows marked improvement out of 340 cases rest of the cases shows mild improvement. Hence Pylorin can be used to manage *H. Pylori* limited dyspepsia.

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Introduction

The complain of dyspepsia is reported thousands of years and stomach related ailments have become dilemma specially in developed country (Moayyedi *et al.*, 2017) The word dyspepsia is the combination of two Greek word “duis” meaning bad and “peptin” means to digest, It commonly refers to indigestion state of the patient but in actual dyspepsia is not associated with indigestion. Upper abdominal pain occasionally linked with meal intake and pathogenesis of gastrointestinal tract is the usual cause. The symptom may last for whole life with recurrent attacks up to 25% of the world population *H. Pylori* positive cases while overweight, some drugs alcohol, tobacco and spice are also contributing factor. (Desai, 2012) This symptom is comprehensively defined as “abdominal pain of recurrent or persistent abdominal pain may be associated with upper alimentary tract other symptoms without bleeding or jaundice for at least a month or more.

Additional symptom may be early satiety, after meal undue repletion and abdominal distention mimic like gastroesophageal reflux disease (GERD) and irritable bowel syndrome (IBS), in the absence of non-erosive condition like duodenal ulcer, GERD, gastric cancer presence of dyspeptic condition is termed as functional dyspepsia (Koduru *et al.*, 2018; TACK *et al.*). Additionally dyspepsia is further divided into sub group on the basis of major ailment presented like in case of pain as major symptom dyspepsia is termed as ulcer-like dyspepsia while in case of abdominal discomfort the dyspepsia is classified as dysmotility like dyspepsia whereas dyspepsia presented with no predominant alimentary track symptom was grouped as unspecified dyspepsia, one another group which is no longer consider named as reflux-like dyspepsia because majority of the patients reflux disease that is treated accordingly. This nomenclature is better applicable for enhanced design of clinical trial performance however its utility is unproven. (Jones, 2019; Talley, 2017). Progressively increasing pattern is observed attendees complaining for functional dyspepsia in gastroenterology medical setup.

Different studies from various part of the world reflect dyspepsia complain frequency ranging 26% to 41%, but only 2%-5% see for medical care in primary health care system while gastroenterologists report 20% to 40% of dyspepsia as major. Dyspepsia burden in terms of quality of life and economic recoil is significant, annually 1.46 billion dollars coast in UK for the management of dyspepsia, same is noted in United States for diagnosis and management of dyspepsia. (Jones, 2019; Vakil *et al.*, 2017) Developing country like Pakistan cannot bear this huge cost, The poly herbal formulation (Pylorin) can be used to manage dyspepsia as an alternate source, which is cost effective, locally developed formulation with indigenous roots, time tested and human tested. This study aims to develop evidence in support of Pylorin clinical efficacy. Similar local studies conducted in varies parts of the world like in Korea Yukgunia-tang was tested for functional dyspepsia and found effective (Ko *et al.*, 2018).

Materials and methods

This study was an experimental clinical trial, case control, open labeled, multicenter evaluation based study to assess anti-Dyspeptic efficacy of poly herbal formulation Pylorin, and randomly patients were assigned to choose either poly herbal formulation or the control placebo. Appropriate clinical history was taken and systemic examination was performed for recording any change on every follow up. All participants were chosen according to the eligibility criteria limitations, for that age ranges between 15-75 years either sex (male and female) can take part in the study, only those participants were enrolled who gave prior inform consent of the their voluntarily participation. More over Patients fulfilling inclusion and exclusion criteria which are mentioned below

Inclusion criteria

The individuals suffering from dyspepsia *infection* were selected on the following basis.

- 1 The individuals suffering from dyspepsia without *H. pylori* infection.
- 2 Individuals having no previous history of *H. pylori* infection.

- 3 Individuals living in Karachi.
- 4 Individuals with no pathological finding on routine examination.
- 5 Individuals from either socioeconomic class including lower, middle and higher.
- 6 Patients having no complications regarding other than GIT system.

Exclusion criteria

The following were the reason for excluding the individuals from this trial:

- 1 Patient with simultaneous physical illness, for example renal dialysis and uncontrolled diabetes mellitus.
- 2 Individuals having stomach or intestinal surgical history were excluded.
- 3 Individuals with past record of any herbal or allopathic medication were excluded
- 4 Individuals with hyper sensitivity history of drug or adverse reaction to any of the study drugs.
- 5 Females with pregnancy were also excluded for the safety measures.
- 6 Individuals with coma, meningitis, and encephalitis or head injury were also excluded.

Settings

This study was conducted on the patients living in the vicinity of Madinat-al-Hikmah, Hamdard University, Shifa-ulMulk Memorial Hospital, Gadap Town Karachi, Hamdard Matab Arambagh Karachi, Saylani welfare trust international head office medical section Bahadurabad, Karachi and Hearbicare Poly clinic Gulshan e Iqbal Block 17, Karachi from March 2016-March 2019.

Protocol

All the patients were explained the purpose of the study in detail and written consent was obtained.

The patient demographic details and baseline clinical features at the time of enrolment were recorded in the questionnaire. So overall, 330 patients were assigned the crude form of the Unani formulation named as Tablet (Pylorin). 2 tablet after lunch and dinner for five weeks 500mg each tablet.

Ethical consideration

Both pre-clinical and clinical study initially approved by the Faculty research committee Faculty of Eastern Medicine for further the approval finally presented to ethical review board of Hamdard University, clearance and permission was given considering the following point under practice throughout the study.

- a) Take consent from each participant after informing participant of the study about the study detail during interviewing and examining the patient who consented to participate in the study.
- b) The data will be kept confidential, identity of the participants will not be revealed.
- c) Medical Superintendent Shifa ul Mulk Memorial Hospital is entitled to excess data at any time.
- d) Animal toxicity of the drug must be rule out before the formal trials on the humans.
- e) Perform Test if *H. pylori* infection suspected particularly.

Outcome

Primary efficacy parameter was clinical response against dyspepsia related ailments the Pylorin response. The secondary efficacy parameter was laboratory investigation to rule out any drug side effects. All the data was analyzed by means of Statistical Package for Social Sciences (SPSS) software and Microsoft excel in order to calculate p value by using Chi Square Test. Statistical test showed difference were consider significant if 'p-value' less than 0.05 calculated.

Safety measurements

Safety of the poly herbal formulation was assessed on the following ground: Information of the adverse events (AEs) and results of monotonous physical examination, Laboratory parameters and clinical vital signs and general physical examination.

Design of Unani Coded Formulation (Pylorin)

The herbal drugs were selected for dyspepsia after extensive literature review which included ancient Unani literature such as Unani Pharmacopeia and published literature from electronic journals. Those

herbs were selected which show ethno-botanical and scientific evidences for the treatment of dyspepsia. Five herbal drugs were selected including *Mallotus philippinensis* (Lam) Muell (Kamela) 150mg, *Curcuma longa* L (Haldi) 150mg, *Psoralea corylifolia* L (Babchi) 100mg, *Piper longum* L (Filfil Daraz) 150mg, *Terminalia chebula* Retz (Halila) 100mg. Powder (*Safoof*) of the above ingredients was used for tablet making.

Collection and identification of plants

The selected herbs for *H. pylori* were purchased from the local market at Joria Bazar. Organoleptic evaluations for the validations of herbal medicines were carried out in the Pharmacognosy department Faculty of Pharmacy, University of Karachi and the voucher specimen number for each herb was allocated: *Mallotus philippinensis* (Lam) Muell (Fruit) MP-06-17, *Curcuma longa* L (Rhizome) CL-03-17, *Psoralea corylifolia* L (Seed) PC-08-17, *Piper longum* L (Seed) VA-07-17, *Terminalia chebula* Retz (Fruite) TC-09-1

Preclinical study

Acute toxicity study was carried out as per OECD guideline on albino mice up to 5000mg/ kg body weight Pylorin was given, no sign of toxicity was observed.

Results

Overall 1550 cases were screened presenting for the complain of dyspepsia during entire duration of

study. Eight hundred and eighty cases were excluded (733 were not meeting the criteria 58 decline to participate and 89 had advance organic disease).

A total of 670 individuals with dyspepsia as predominant complain without active organ disease sign and symptom on through clinical examination were allocated treatment for the final analysis. Group A (n=330) received test drug Pylorin out of these 4 patients did not continue due to allergy attack, further more five patients lost follow up due to travel abroad and 3 patients discontinued intervention due to personal busy schedule, one individual was excluded due to missing data finally three hundred and seventeen individuals data was analyzed. Another group B (n=340) was also allocated intervention but out of these 2 patients did not receive allocated intervention to allergic attack 6 patients lost to follow-up due to transfer of job and 10 patients discontinued intervention complain of drug not effective 2 patients were more excluded due to missing data finally 320 patients data were analyzed. 733 cases infected with *H. Pylori* resulting prevalence 53% of infection with bacterium in patients with dyspepsia without significant finding of other alimentary track disease sign on clinical examination whereas 670(53%) cases without infection reported dyspepsia. The mean progression time for the development of dyspepsia recorded in the history of the patents proforma reflect the similar duration (38.1 month in cases of *H. Pylori* infection and 37.8 month in case on non-infective p= NS).

Table 1. Age distribution of Patients.

Class Intervals	Total Patients	Pylorin		Placebo		
		Male Patients	Female Patients	Total Patients	Male Patients	Female Patients
15 ---20	21	16	5	11	6	5
21--- 25	28	20	8	29	22	7
26 --- 30	38	24	14	40	32	8
31 --- 35	53	30	23	51	40	11
36 ---40	58	50	8	52	43	9
41 ---45	61	51	10	58	40	18
46 --- 50	20	18	2	35	21	14
51 --- 60	28	27	1	31	15	16
61 --- 65	10	8	2	13	5	8
Total	317	244	73	320	224	96

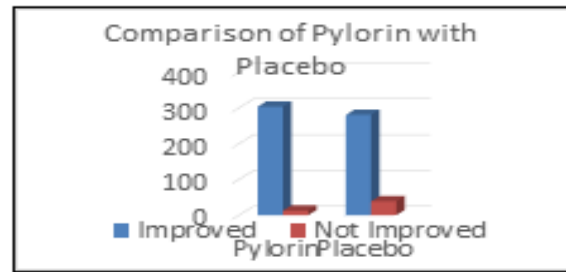
Both group shoes similar pattern in relation to involvement of gender both gender , positive finding of previous family history for functional or visceral GIT disease, additionally positive history of tobacco consumption, alcohol use, previous surgery for abdomen, personal history of drug allergies and aesthetic surgeries.

Mean age of all the participants was 35 years majority of the study subject's fall between age group 30-45years (table 1). Outcome of the treatment after 5

week duration was comparable 304 cases recovered out 317 in case of pylorin whereas 281 cases got relief with the use of placebo (table 2). Frequency of therapeutic improvement was highest in case of Pylorin group, 265 subjects got mild improvement on contrary only 27 subjects fall in marked improvement category. moderate improvement seen in 254 patients in case of placebo recipients while 39 cases from Pylorin group only 13 subjects show mild level of improvement from the same formulation and 39 with placebo as shown in the outcome (table 3).

Table 2. Comparison of Pylorin with Placebo.

Improvement Scale	DRUGS		p Value
	Pylorin	Placebo	
Improved	304	281	0.001
Not Improved	13	39	
Total	317	320	



The frequency of Hyperacidity was recorded in 216 participants 34.0% while heart burn and reflex esophagitis seen in 268 cases 42.0%, higher than the any symptom while GERD was noted in 153 cases 24% of all individuals with lowest frequency among all ailments reported as shown in diagnosis (table 4).

Over all 270 males were enrolled 42% while 367 females 58% took part in the study as shown in

gender (table 5). There was no other major system symptoms reported under adverse drug reaction like headache 2%, mood swings 3%, Numbness or tingling sensation 1%, dizziness 1% and Depression like symptoms were reported by 3 % of the cases, history of mild to moderate degree of chest pain and palpitation were reported by 2 % of the all enrolled cases, less than 1% of the cases reported for sexual changes under test drug.

Table 3. Outcomes.

Valid		Frequency	Percent	Valid Percent	Cumulative Percent
		Pylorin/Placebo			
	Mild improvement	13/39	4.0/12	4.0/12	4/16
	Moderate improvement	39/ 254	12/84	12/84	16/100
	Marked improvement	265/27	84/8	84/8	100/4.0
	Total	317/320	100.0	100.0	

Discussion

Current study show functional dyspepsia can be manage efficiently with Pylorin as compared to

placebo in non-gastric ulcer and *H. Pylori* associated dyspepsia, whoever frequency of *H. pylori* is found up to 53% in patients reporting for the complain of

dyspepsia.

Although dyspepsia latterly means difficulty in digestion it is derived from two Greek words “ diues” means bed and “peptin” means to digest both these words are poor explanatory for dyspepsia because there is no difficulty in digestion but upper abdominal ailments most often after taking food due to the abnormality in upper abdominal track system. It is not a disease but a symptom that may last for varying

period of time even for life time in some cases persist as fluctuating course(Desai, 2012, Barbara *et al.*, 1989).

Dyspepsia is also refers for presence of symptom(s) like early satiation, burning and upper abdominal pain other gastroenterological symptoms may coexist including bloating and nausea but they are non-specific so they are not part of the definition (Harmon and Peura, 2010).

Table 4. Diagnosis.

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid				
Hyperacidity	216	34.0	34.0	34.0
Heart burn and reflex esophagitis	268	42.0	42.0	76.0
GERD	153	24.0	24.0	100.0
Total	637	100.0	100.0	

This study find frequency of dyspepsia up to 47% whereas worldwide it is recorded 26-41% among these only 25% cases seeks for medical attention, dyspepsia accounts for 5% of all people taking medical consultation it comprise up to 40% of all gastroenterological OPD seeking individuals, in primary healthcare setup dyspepsia is more easily handle with proton pump inhibitor and regimens against *H. pylori*. (Jones, 2019) Pylorin tablet is equally effective for the management of dyspepsia observed in current study. Economic burden in terms of affected quality of life, diagnosis and drug costing for the management of dyspepsia reported as UK 1.46 billion dollars same in USA and a Swedish study estimated 26 million pounds for 8million population (Jones, 2019), our study estimated Pylorin cost less than 10 dollars per patient it is may be due to availability of indigenous raw material. Some new

treatment options include Acotiamide, tandospirone and rikkishito are finalized in 11 annual meeting of Japan society of Gastroenterologist under discussion different thematic area from 2015- 2017 referring to revised Rome IV classification, with minor changing just to enhance specificity of the criteria include the development of nausea after meal in association with predefine symptoms like postprandial fullness and epigastria burning (Suzuki, 2018). Many randomized clinical trials have been conducted so far, peppermint and caraway are the constituent part of formulations they show remarkable results (60-90% recovery) safety profile of most of them is missing (coon and Ernst, 2002) current study is conducted keeping in consideration the safety profile in association with efficacy against dyspepsia management, after applying Chi-square test (p value 0.001) significant difference was observed between Pylorin and placebo.

Table 5. Drugs * Sex Cross Tabulation (Male and Female).

Treatment	Gender		TOTAL
	Female	Male	
Placebo	96	224	320
	30 %	70 %	100.0%
Pylorin	73	244	317
	23%	77%	100.0%
Total	169	468	637
	26.5 %	73.5 %	100.0%

It is concluded that Pylorin tablets is reliable treatment option for the management of dyspepsia.

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