



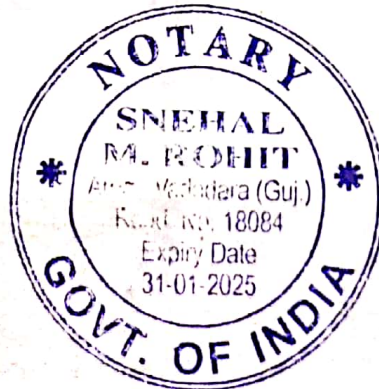
सत्यमेव जयते

INDIA NON JUDICIAL Government of Gujarat Certificate of Stamp Duty

Regd.No.: 109.

Date: 27/1/2022

Certificate No. : IN-GJ88199102871587U
Certificate Issued Date : 10-Jan-2022 04:37 PM
Account Reference : IMPACC (SV)/ gj13116604/ BARODA/ GJ-BA
Unique Doc. Reference : SUBIN-GJGJ1311660409922607714989U
Purchased by : RANJIT MALI
Description of Document : Article 5(h) Agreement (not otherwise provided for)
Description : Not Applicable
Consideration Price (Rs.) : 0
(Zero)
First Party : VITAL CARE PVT LTD
Second Party : PARUL INSTITUTE OF AYURVED
Stamp Duty Paid By : VITAL CARE PVT LTD
Stamp Duty Amount(Rs.) : 300
(Three Hundred only)



IN-GJ88199102871587U

KC 0022264847

Statutory Alert:

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2. Any discrepancy in the details on this Certificate and as available on the website / Mobile App renders it invalid.
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4. In case of any discrepancy please inform the Competent Authority.



Regd.No.: 109.
Date: 27/1/2022

MEMORANDUM OF UNDERSTANDING (MoU)

This Memorandum of Understanding (hereinafter called as the 'MOU') is made and executed at Vadodara on this day 11th day of January 2022, between **In-House R&D Unit a part of Vital Care PVT. LTD.**, an Ayush premium mark, ISO and GMP certified company established in 1992, having registered manufacturing unit at plot No.361, 362, Ramangamdi, Por GIDC, Vadodara. Herein after referred to and called as 'SPONSOR'.

Parul institute of ayurved and research, Ishwarapura Parul University represented herein by its name of competent authority **Dr B G Kulkarni** Principal hereinafter referred as 'INSTITUTE' and has fully established hospital facility for clinical studies in the field of ayurveda.

Whereas, the sponsor is an ayurveda company involved in manufacturing of Ayurvedic medicines and in-house well established DSIR recognized Research and Development centre.

Whereas, the SPONSOR and INSTITUTE are concerned with the diagnosis, treatment and prevention of disease or clinical research for improvement of health care.

The parties represent and warrant that they each have the authority to enter into this MoU. In consideration of the undertakings and commitments set forth herein, the parties agree to enter into this collaborative clinical research project MoU.

PROTOCOLS

The scope and nature of the project to be performed will be in accordance with the protocol agreed between the SPONSOR and INSTITUTE. "Protocol" means the document signed by the authorized representative of the INSTITUTE, detailing all aspects of the collaborative research project. This protocol consist details of study activities and responsibilities to be undertaken.

OBLIGATIONS

INSTITUTE and the SPONSOR agree to provide the afore stated protocols as per Annexure I accompanied by services referred above at the onset for the following clinical research project of the SPONSOR entitled:-

Project Title: Evaluation of efficacy and safety of Peggard syrup in comparision with Digene syrup in *Amlapitta*- an open labelled, randomized, two-arm, prospective, parallel clinical study.

INSTITUTE shall prepare final report in written and publication of the manuscript based on the data obtained.

The SPONSOR shall be responsible for providing the fund required for the project as per annexure II as mutually agreed between the parties.

PAYMENT

Total cost of the project would be as agreed upon by both the parties. Payment shall be made by the SPONSOR to the INSTITUTE in the favour of Parul Institute of Ayurved And Research.



CONFIDENTIALITY & INTELLECTUAL PROPERTY

Each Party shall keep confidential, and not disclose and shall cause its agents and employees not to disclose, to any third person or make any unauthorized use of any technical, economic, financial, marketing or other information received, discern or generated either in writing or orally in connection with this Agreement or the performance hereof.

Notwithstanding the foregoing, it is agreed that the Parties may disclose information: (a) if and to the extent required by law or government regulations; and (b) to their legal or other advisers solely for the purpose of obtaining advice in connection with this Agreement and subject to appropriate confidentiality obligations. The obligations imposed by this Article shall survive the termination of this Agreement for three (3) years after such termination, unless such information becomes part of the public domain without any act or omission by it.

VITAL CARE, by virtue of being a research organization and specializing in pharmaceutical development in particular, has developed many products and the ownership of the existing products in terms of IP will continue to rest with VITAL CARE.

Parul institute of ayurved and research, by virtue of being a research institute, has developed many products and the ownership of the existing products in terms of IP will continue to rest with Parul institute of ayurved and research, unless additional or new patentable facts are discovered during the course of conducting specific projects in collaboration with VITAL CARE.

However, Sponsor company / institute has all rights for selection and execution of IPR related to collaborative work.

All research information arising as an outcome of collaborative research will have joint publications. However, sponsor will hold rights to decide the type of publication and selection of journal(s).

DURATION AND TERMINATION

The period of the duration of this Agreement is three (3) years. This agreement shall be considered to enter into another term of 3 years unless the party sends written notice to the other within 30 days before the end of the agreement.

Either Party hereto may terminate this Agreement forthwith by written notice to the other Party, upon the occurrence of any of the following:

- if such other Party fails to perform any of its materials obligations under this Agreement and such failure is not solved within 30 days after notice thereof;
- if any petition in bankruptcy or for other relief under any law of any jurisdiction, relating to bankruptcy, insolvency, reorganization or relief of debtors should be filed by or against such other party, or if such Party commits an act of bankruptcy or should be adjudicated insolvent, or should a receiver, trustee or similar person be appointed with respect to all or a substantial portion of the assets of such other Party;
- if such other Party should be merged into or consolidated with any third party, or the ownership, management or control of such other Party should be in mutual contest in writing before 30 days prior to incorporation of any third party / management.



- if any condition or event constituting Force Majeure as provided herein should prevent either Party from fulfilling its obligations for more than one consecutive month; or
- if such other Party for any reason discontinues or suspends or any Agreement or contract between Parties and should be terminated.

Both Parties represent that there are no claims, demands or causes of action pending against it or any of its subsidiaries or affiliates that would entitle it to be indemnified under this article and to the best of its knowledge, no such claim, demand or cause of action is threatened.

ADJUSTMENT OF DIFFERENT OPINIONS

Parties shall attempt to settle the unspecified or disputed matters relative to this Agreement in good faith through amicable negotiations.

GOOD FAITH NEGOTIATION

Or in relation to this Agreement through mutual and amicable discussion and good faith negotiation between the parties.

COMPETENT COURT

This agreement shall be governed by and construed in accordance with the laws of India, without regard to the conflict of law principles thereof. The parties agree to submit to the jurisdiction of the principles thereof.

The parties agree to submit to the jurisdiction of the competent court located in Vadodara, Gujarat.

ADMINISTRATION OF INFORMATION MATERIALS

Each Party shall take necessary measures to preserve the records of safekeeping by reproductions and copies in order to avoid any loss or damage or theft or leak of all of information materials including electronic data provided by the other Party.

Each Party shall return all reference materials or information including electronic data provided by the other Party to the other Party immediately upon termination of this Agreement.

Publications and presentations

It is the intent of the parties that no publication shall contain any of confidential information disclosed by the SPONSOR without SPONSOR'S prior written permission. No data shall be published without prior written consent from the SPONSOR.

COMMUNICATION

All communication required to be served the purpose of collaboration will be carried out at one end point through the following representative of both the parties.

Behalf of VITAL CARE PVT.LTD: MR.SANKALP AGRAWAL

Behalf of Parul Institute: DR. B.G. KULKARNI



ANNEXURE I

Project Title: Evaluation of efficacy and safety of pepgard syrup in comparison with Digene syrup in *Amlapitta*- an open labelled, randomized, two-arm, prospective, parallel clinical study.

The details like AIM, methodology, analysis criteria are mentioned below for the clinical trial on effect of Peggard Syrup in Hyperacidity.

INTRODUCTION

The GIT is one of the important systems in the body. Processes like ingestion, digestion of food, absorption of digested food and excretion of undigested food are involved in obtaining nutrition. According to Ayurvedic point of view reduced digestive fire (mandagni) is the mother of all diseases including disorders of GIT.¹ The GIT is one of the major and commonly used routes for drug administration. Being an organ for digestion and also major route for drug administration continuous assault on this system leads to diseases and toxic effects.

Hyperacidity, gastric ulcer, gastritis (inflammation of the lining mucosa of stomach), gastrectasia, post-gastectomy syndrome (patient feels faint, weak and nauseous with rapid pulse), pyloric stenosis (narrowing of muscular outlet of the pylorus), pylorospasm (closure of outlet of stomach) can be considered as important diseases of the stomach.²

The modern approach to control gastric ulcer is mainly to inhibit gastric acid secretion by histamine-H₂ receptor blocker (ranitidine, famotidine etc.) and proton pump inhibitor (omeprazole, lansoprazole etc.) or to eradicate *Helicobacter pylori* infection by antibiotic (Metronidazole, amoxicilline, clarithromycine etc.). Considering the several side effects (arrhythmias, impotence, gynaecomastia and hematopoietic changes) of modern medicine, indigenous drugs possessing fewer side effects should be looked for as a better alternative for the treatment of peptic ulcer.³

In traditional Indian medicine, several plants have been used to treat gastrointestinal disorders, including gastric ulcer and the phytochemical analysis of these plants has yielded a number of compounds with gastro-protective activity.⁴

AIM:

To evaluate efficacy and safety of Peggard syrup in comparison with Digene syrup in *Amlapitta*- an open labelled two armed clinical trial for functional dyspepsia.

RATIONALE


The study involves the evaluation of Peggard syrup in the management of hyperacidity, functional dyspepsia and gastritis. Peggard is the poly herbal formulation, which is formulated with ingredients that are classically mentioned for treating acidity, ulcers, healing mucosal tissue and maintaining the digestive fire. Its therapeutic action could be understood and well documented.

REVIEW OF LITERATURE

Disease review

• Modern

Peptic ulcer disease is a group of disorders characterized by the presence of ulcers in any portion of gastrointestinal tract (GIT) exposed to acid in sufficient concentration and duration. Although these ulcerations most commonly occur in the stomach (gastric ulcer), or small intestine (duodenal ulcer), this disease also includes Barrett ulcer of the oesophagus (Barrett's oesophagus or Barrett's metaplasia) and other upper GI ulcers: Gastric acid hyper secretion and gastro



duodenal or gastro esophageal ulcers, due to stress are very common human sufferings today in the world of globalization. The pathophysiology of acid gastric diseases is attributed to the imbalance between aggressive factors (like acid, pepsin and *Helicobacter pylori* infection) and defensive factors (like secretion of mucous, bicarbonate and prostaglandin) ⁵. Hyper secretion of acid is pathological condition, which occurs due to uncontrolled secretion of HCl from the parietal cells of the gastric mucosa through the H⁺-K⁺ ATPase proton pump. Hyper secretion of acid aggravates the gastro-duodenal ulcers by loss of gastro protection by various factors.⁶

Helicobacter pylori infection is the most common cause of peptic ulcer proved by isolation of *H. pylori* from stomach of patients with gastritis and peptic ulcer. ⁷ From that earliest times chalk, charcoal and slop diets had been noted to provide the symptomatic relief from dyspepsia but little rational therapeutic intervention was available for the treatment of gastro duodenal ulcerations. In the 17th century chalk and pearl juleps were utilized for infant gastric disorders.

- Ayurveda

Amlapittais composed of two words i.e. *Amla* & *Pitta*. The term *Amla* is as significant as a special type of taste has the similarity with sour taste which causes excessive salivation & also a typical natural property of *Pitta* which is a bodily chemical substance mainly responsible for the maintenance of the process of digestion, transformation & transmutation. *Acharya Sushruta* mentioned that *Amla* is the property of *vidagdha Pitta* (fermented). Regarding the clinical definition, the disease has the following symptoms like *avipaka* (indigestion), *klama* (exhaustion), *utklesha* (nausea), *tikta-amlaudgara* (eructation with bitter & sour taste), *gaurava* (feeling of heaviness of the body), *hrit-kantha-daha* (burning sensation in the chest & throat), *aruchi* (loss of appetite) is termed as *Amlapitta*. *Amlapitta* is considered to be a gastrointestinal disorder caused due to suppression of *jatharagni* (gastric fire).

Preclinical Study:

Standardization and Pharmacological activity of "Peggard Syrup": A polyherbal formulation, dissertation work was carried out at Shri B.M Shah College of Pharmaceutical Education and Research, Modasa. Anti-ulcer activity was performed on Wistar albino rats after getting clearance from IAEC which was a part of the dissertation work. Results obtained showed that microbial load, heavy metal were within the prescribed limits.

Anti-ulcer activity:

Antiulcer activity was carried out using Wistar albino rats and giving 100 mg/kg aspirin (disease control), 100mg/kg ranitidine (standard drug), and 1ml/kg, 2 ml/kg and 4 ml/kg peggard syrup. Results obtained for ulcer Index and histopathology revealed that peggard syrup has dose dependent Anti ulcer activity, which may be due to the presence of phytoconstituents like saponin, flavonoid, tannin alkaloid, glycoside, Carbohydrates and triterpenoids in the syrup.⁸

RESEARCH DESIGN

Prepared peggard syrup along with quality control parameters documents will be provided by Vital Care Pvt. Ltd. Reference standard Digene syrup will also be provided by the company. The details pertaining to raw materials utilized, finished product analysis, heavy metal analysis and microbial analysis will be provided by the company.

Clinical study methodology

Patients will be screened for signs and symptoms of *Amlapitta*. The research protocol is to be approved by Institutional Ethics Committee (IEC) and registered in Clinical Trials Registry of India (CTRI). An informed consent from each enrolled patient will be obtained before commencement of the treatment. If required than only sonography would be conducted on the



doubtful patient for determining presence or absence of peptic ulcers.

The following criteria will be followed for selection of patients to be enrolled.

Plan of Clinical Study:

Inclusion criteria

- Patients of 21–60 years age
- Presence of *Pratyatmaka Lakshanas* (cardinal symptoms) of *Amlapitta* such as *Avipaka* (indigestion), *Klama* (exhaustion without any exertion), *Utklesha* (nausea), *Tikta-Amlodgara* (erectations with bitter or sour taste), *Gaurava* (feeling of heaviness of the body), *Hrit-Kanthadaha* (burning sensation in the chest and throat), and *Aruchi* (loss of appetite)
- Chronicity <1 year
- Patients with gastritis, gastric erosion.

Exclusion criteria

- Chronicity >1 year
- Patients having any systemic disorders such as hypertension, diabetes
- Patient with gastrointestinal complications such as peptic ulcer, duodenal ulcer, perforation, stenosis, bleeding, malaena, and malignancy.

Grouping and posology Total 36 patients will be registered and divided into two groups comprising of 18 patients in each. Group A, will be administered modern medicine Digene syrup, and Group B, will be administered peggard syrup.


Diagnosis criteria

Amlapitta Symptom Rating Scale (ASRS) will be used for diagnosis criteria.

Criteria for assessment

Assessment will be done on the basis of improvement in signs and symptoms of the *Amlapitta* on the basis of specific scoring pattern. ASRS scale will be used as assessment scale.⁹

Grading score	0	1	2	3
Avipaka (indigestion)	No indigestion	Indigestion on only by heavy food.	Delayed digestion of lighter food	Impaired indigestion of even lighter
Gaurav (lethargy)	No lethargy	Occasional but can do daily work	Continuous tiredness that hampers daily work	Due to tiredness avoid any routine work
Utklesha (nausea)	No salivation	Occasional but not daily	Daily and after taking solid food for sometime	Frequently and feel Amlata
Tikta Amla Udgara (acid eruption, belching)	No Tikta	Appears 1-5 times/day only on consumption of sour and spicy food	Appears 6-10 times/day on the consumption of any type of food	Appears 10 times/day on the consumption of any type of food
Gurukoshthatwa (heaviness in abdomen)	No gurukoshthtwa	Occasional with a normal quantity of food	Continuous while taking normal food	Continuous while taking less food



			with an average quantity	
Aruchi (anorexia)	No Aruchi	Patient feels aruchi but takes food time to time	Patient sometimes takes food and sometimes avoid it	Patient avoids the food many times
Vibandh (constipation)	No Vibandh	Intermittent relieved by pathya ahara vihar	Continuous relieved by mild laxative (Mrudu Virechan)	Continuous only relieved by strong medication (Teekshan virechan)
Shirorujah (Headache)	No headache	Intermittent reliever by pathya	Continuous not relieved by medicine	Continuous only relieved by medicine

Lab Investigations

It is inclusive of only blood investigations including CBC, ESR and RBS.

Therapy duration

Group A will be administrated digene syrup for adults- 2 teaspoons (10ml each), before lunch and dinner

Group B will be administrated 2 teaspoons (10ml each), 2 times, before lunch and dinner.

The patients will be administrated medicine for 30 days and three follow ups will be taken 1st follow up on 16th day, 2nd follow up on 30th day and 3rd follow up will be on 45th day.

Assessment of overall effect of therapy

The total effect of therapy will be assessed considering overall improvement in sign and symptoms.

- Complete remission: 100%
- Marked improvement: 76–99%
- Improvement: 51–75%
- Mild improvement: 26–50%
- Unchanged: Below 25%.

Statistical analysis

Appropriate statistical method for analysis will be applied like parametric (paired/unpaired T-test) or non parametric (Friedman test) test or ANOVA will be applied.

References:

1. Srikantmurthy KR. Vagabhatas Ashtanga Hridya Vol. II., Krishnadas Ayurveda series- 27: 113-114.
2. Soumya MN, Nanjammani N. A Phytochemical analysis of seedless amalaki fruit (*Embllicaofficinalis*) churna. International Journal of Pharmaceutical Science Invention 2017;6:09-12.
3. Akhtar MS, Akhtar AH, Khan MA. Antiulcerogenic effects of *Ocimum basilicum* extracts, volatile oils and flavonoid glycosides in albino rats. International Journal of Pharmacognosy 1992; 30:97-104.
4. Satyavati GV, Gupta AK, Tondon N. Medicinal plants of India. Vol II, New Delhi (India): Indian Council of Medical Research; 1987. pp. 574.



5. Jain KS, Shah AK, Bariwal J, Shelke SM, Kale AP, Jagtap JR, Bhosale AV. Recent advances in proton pump inhibitors and management of acid-peptic disorders. *Bioorganic and Medicinal Chemistry* 2007;15:1181-1205.
6. Bandyopadhyay U, Biswas K, Sangupta A, Moitra P, Dutta P, Sarkar D, et al. Clinical studies on the effect of Neem (*Azadirachta indica*) bark extract on the gastric acid secretion and gastro-duodenal ulcer. *Life Sciences* 2004; 75:2867-2878.
7. Marshal B, Warren JR. Unidentified curved bacillus in active chronic gastritis. *Lancet* 1983; 1:1273-1275.
8. Dissertation work (project sponsored).PI- Dr. NM Patel. Standardization and Pharmacological activity of 'Peggard syrup': A polyherbal formulation. Pharmacognosy, Shri BM Shah College of Pharmaceutical Education and Research, Modasa.
9. Khapre M, Nautiyal V, Jagzape M and Saxena V. Effectiveness of Ayurveda treatment in Urdhwaga Amlapitta: A clinical evaluation. *Journal of Ayurveda and Integrative Medicine* 12 (2021) 87-92.





ANNEXURE II
TOTAL BUDGET ALLOCATION

No.	Expenditure Head	Total Expenditure (Rs.)
1	EC Review Fees.	10000.00
2	Investigator Charges (PI)	30000.00
3	Co-Investigator Charges (Co-PI x 2)	60000.00
4	Lab Investigations (Blood Investigations – CBC, ESR, RBS)	5000.00
5	Institutional Charges	15000.00
6	Statistician charges	20000.00
7	Publication Charges	10000.00
8	Miscellaneous Charges	10000.00
	Total	1,60,000.00

Investigators involved

Sr. No.	Investigator	Name	Sign
1.	Principal Investigator	Dr. Vaishali Deshpande	<i>Vaishali Deshpande</i> 20/01/2022
2.	Co Investigator	Dr. Bhavin Dhanavade	<i>Bhavin Dhanavade</i> 20.01.22
3.	Co Investigator	Dr. Naresh Kore	<i>Naresh Kore</i> 20.01.22



IN WITNESS WHEREOF, the Parties hereto have caused this Agreement to be executed as of the date written above.

AGREED:



For

Parul Institute of Ayurved & Research

Authorized Signatory

DR. B.G. KULKARNI

20-1-22



For

VITAL CARE PVT. LTD.

Authorized Signatory

MR. SANKALP AGRAWAL

20-1-22

Name of Institution	Name of Industry
PARUL INSTITUTE OF AYURVED AND RESEARCH	VITAL CARE PVT. LTD.
Ishwarapura	361-362, GIDC- POR, RAMANGAMDI
P.O: Limda, Waghodia, vadodara, Gujarat	VADODARA- 391 243
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Web: www.paruluniversity.ac.in/piar	Web: www.vitalcare.co.in

Witness 1: *20-01-22*

DR. PRASANNA MATHAD



Witness 2:

DR. SWITU JANI



Witness 3:

DR. VAISHALI DESHPANDE

20/01/2022



Witness 4:

DR. GAUTAM FICHADIYA

20/1/22



ATTESTED

S.M. Rohit
S. M. ROHIT
NOTARY (Govt. of India)
27/1/2022



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