

An Open Labelled Single Arm Clinical Study to evaluate the Efficacy and safety of Grace Hing (Hing oil 15mg) HPMC Capsules in Primary Dysmenorrhea.

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Highlights of the findings and novelties:

- ✓ Great relieve for primary dysmenorrhic women
- ✓ Improve health related quality of life.
- ✓ Safe capsule without any adverse effect

Type of Article: Original Research article (clinical study)

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Section: Natural Products

Taxonomy: Disease (Primary dysmenorrea), **Methodology** (open labelled, single arm clinical study)

This study was conducted in compliance with the final protocol, the applicable Harmonized Tripartite Guidelines for Good Clinical Practice (GCP), the relevant sections of Good Laboratory Practice (GLP), local laws and regulations, and the provisions of the Declaration of Helsinki.

ABSTRACT

Background: Many women are suffering from hormonal imbalances. Primary Dysmenorrhea is one of the new potential threats in today's world. While most women experience minor pain, dysmenorrhea is diagnosed when the pain is severe to limit normal activities or requires medication. Ayurveda shines a light on potential factors that can increase menstrual pain and remedies that can not only reverse the pain but increase the overall feeling of wellbeing. Recent studies have shown numerous promising activities of medicinal plants.

Aim: This study is an attempt to explore and assemble the various pharmacological actions of the hing oil of *Ferula asafoetida* reported during the treatment of primary dysmenhorrea

Material and method: A total of 15 female aged 15-35 years with dysmenorrhoeal pain participated in this study. By assessing vas score, the Verbal Multidimensional Scoring System (VMSS), the SF-36 questionnaire for Health-related Quality of life (HRQoL), efficacy assessment on menstrual blood loss by pictorial blood loss assessment score, associated systemic symptom and usage of analgesics.

Result and conclusion: According to our investigation GRACE HING (Hing oil 15 mg) HPMC Capsules represents a safe, effective treatment for menstrual pain, its associated systemic symptoms and to improve health-related quality of life.

KEYWORDS: Effective, Medicinalplant (*Ferula asafoetida*), menstrual pain, statistical data, women

1. INTRODUCTION

Menstruation is one of major sign in women's healthy reproductive and endocrine system. It is a natural phenomenon as a part of the natural progress of reproductive life in women. The same menstruation can cause problems if it is associated with unbearable pain causing dysmenorrhea.¹ Plants have been a consistent source of remedy and these days, much prominence has been placed on discovering curative agents from medicinal plants. Nowadays a number of people chose to use medicinal plants instead of chemical drugs.⁴

Asafoetida (*Ferula asafoetida*) also known as hing, Devil's drug, ferula, food of Gods, incense of Devil, stinking gum is an important spice crop belonging to family Apiaceae. It is native to Iran and Afghanistan. Its dried latex (gum oleoresin) is generally used for flavouring curries, sauces, and pickles.³ it is specially considered an ailment for women. It is used as a treatment of

several problems such as unwanted abortion, unusual pain, sterility, difficult and excessive menstruation and leucorrhoea.⁵

A study was performed to investigate acute and sub chronic oral toxicity of Ferula asafetida gum (28 days) in Sprague Dawley rats. The result of this data showed that oral intake of Ferula extract in rats for 28 successive days had no significant changes on body weight, and haematological parameters in rats all during the period of the experiment, and there were no significant increases in the activity of aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, creatinine and urea. Mild changes like thrombosis and sinusoidal leukocytosis, portal infiltration with inflammatory cells were seen in liver of the rat treated with it, while there kidney showed reduction of the capillaries in the glomerulus, Bowman capsule become broader and deeper, and damage to tubule cell of kidney, widening of renal blood vessels. This revealed that ferula had wide safety range with little toxicity for short term use in dose of 250 mg/kg.⁸

The volatile oil (3-17%) consisting of disulfides as its major components, notably 2-butyl propenyl disulfide (E- and Z-isomers) with monoterpenes (α - and β -pinene, etc.), valeric acid, free ferulic acid, and traces of vanillin. The disagreeable odour of the oil is reported to be mainly due to the disulphide C₁₁H₂₀S₂. It also contains triterpenoids and saponins. Asafetida consists of resin (40-64%), gum (25%) and essential oil (10-17%) as three main constituents. Thus due to its hepatoprotective and digestive enzyme activity, Hing has the potency to subside the abdominal pain due to physiological/ metabolic disturbances.¹⁰

Grace Hing oil capsules are 100% vegan and natural supplement. Grace Hing oil capsules are a prominent medicinal product for abdominal swelling and a pain due to gas in intestine. It stimulates the secretion of a lot of digestive enzymes and trigger healthy digestion with no loss of nutrition. Hing or asafetida is rich in free radical scavengers and give multiple benefits including relieving menstrual pain. The present study is initiated with an aim to identify the safety and Efficacy of Grace Hing oil (resource of the medicinal plant Asafetida) for certain gynaecological troubles called primary dysmenorrhoea.

1.1. STUDY OBJECTIVE

The main purpose of this study is to evaluate the Efficacy of Grace Hing (Hing oil 15mg) HPMC Capsules in Primary Dysmenorrhoea, to evaluate the safety of Grace Hing (Hing oil 15mg) HPMC Capsules in Primary Dysmenorrhoea, to assess the improvement in the quality of life

determined by SF- 36 health survey questionnaire, and to assess the reduction in the duration of pain.

2. MATERIAL AND METHODS

This is an Open Labelled Single Arm Clinical Study to evaluate the Efficacy of Grace Hing (Hing oil 15mg) HPMC Capsules in Primary Dysmenorrhhea subjects. A total of 15 female aged between 15-35 years with dysmenorrhheal pain participated in this study. All cases were identified as primary dysmenorrhhea based on their menstrual history, ultrasound and physical examination performed by a gynaecologist.

Subjects with Primary Dysmenorrhhea were allocated and provided to receive Grace Hing (Hing oil 15mg) HPMC of 2 Capsules per day for Period of 2 cycles and assessments were conducted. The primary outcome was pain intensity reduction measured by a Visual Analog Scale (VAS). All participants were evaluated and treated on the first day of their period. The procedure was fully explained to the participants and they were requested to sign the consent form. All assessments were performed at baseline, each menstrual cycle during the treatment course and the follow-up course. Any adverse events had been recorded throughout the study. The study protocol and the patient information sheet(s) were reviewed and approved by the appropriate Independent Ethics Committee ,Pharexcel Consulting Private Limited ,11, 10th Cross, AYR lay out, Shettyhalli, Jalahalli West, Bangalore -560015. Written informed consent was obtained from subject(s) before the start of the trial and after the approval from IEC. Ethics Committee notifications as per the GCP guidelines issued by the Central Drugs Standard Control Organization and ethical guidelines for biomedical research on human subjects issued by the Indian Council of Medical Research were followed during the conduct of the study.

2.1. STUDY SETTING AND POPULATION

The study was conducted at NRR Hospital Janapriya Apartments 3&3A, Hesarghatta Main Rd, Next to, GeleyaraBalaga Layout, Jalahalli West, Bangalore, Karnataka 560090 from 10-May-2022 to 24-Aug-2022 .A total of 15 female aged between 15-35 years with dysmenorrhheal pain participated in this study. All cases were identified as primary dysmenorrhhea based on their menstrual history;all necessary examinations have done by a gynaecologist.

Subjects with a known allergy to any of the study medication, co-existing illness, current or past history of severe gastritis, secondary dysmenorrhea, pelvic inflammatory disease, acute or recurrent urinary tract infection, adnexal masses, uterine fibroids, endometriosis, adenomyosis that in the opinion of the Investigator would impact patient safety and/or the study data were not eligible to participate in the study

2.2. DATA ANALYSIS

Demographic characteristics and result of the study were summarized with summary statistics including average and Standard deviation (SD) for continuous variable and frequency and percentages for categorical variable. Any AEs will be summarized with a number and the percentage. At the time of evaluation, the most suitable method was chosen into best represent the study objective.

3. RESULTS

In this study total of 15 female aged 15-35 years with dysmenorrheal pain were screened and then enrolled for the study after satisfying the inclusion-exclusion criteria.

3.1.EFFICACY ASSESSMENT OF PAIN INTENSITY (VAS SCORE)

MEAN DATA OF VAS SCORE

The Average score of pain intensity in before usage of GRACE HING (Hing oil 15 mg) HPMC Capsules is 6.87 ± 1.46

The Average score of pain intensity in cycle 1 after usage of GRACE HING (Hing oil 15 mg) HPMC Capsules is 2.73 ± 2.66 , cycle 2 is 1.40 ± 1.59 , cycle 3 is 1.47 ± 1.55

The study on Pain intensity demonstrated that the pain reduction started immediately after starting the treatment and continued to decline in the subsequent three consecutive (post cycle 1, post cycle 2, post cycle 3) menstrual cycles.

3.2.EFFICACY ASSESSMENT OF VERBAL MULTIDIMENSIONAL SCORING SYSTEM (VMSS)

The Verbal Multidimensional Scoring System (VMSS) is assessed to evaluate the working ability, the systemic symptoms and whether analgesia is required or not

Parameter	Working ability	Systemic symptoms	Analgesics requirement
Baseline assessment	2.27±0.88	1.87±0.83	2.07±0.80
Post cycle 1	0.53±0.52	0.60±0.51	0.27±0.46
Post cycle 2	0.40±0.51	0.47±0.52	0.13±0.35
Post cycle 3	0.33±0.49	0.40±0.51	0.20±0.41

Table 1: EFFICACY ASSESSMENT OF VERBAL MULTIDIMENSIONAL SCORING SYSTEM (VMSS)

As shown in (table 1), the study on Verbal Multidimensional Scoring System (VMSS) on work ability of the subjects have been improved immediately after starting the treatment in subsequent three consecutive (post cycle 1, post cycle 2, post cycle 3) menstrual cycles.

The study of Verbal Multidimensional Scoring System (VMSS) on systemic symptoms and Analgesics requirement have been reduced after starting the treatment in subsequent three consecutive (post cycle 1, post cycle 2, post cycle 3) menstrual cycles.

3.3.EFFICACY ASSESSMENT ON HEALTH- RELATED QUALITY OF LIFE BY SF-36 PATIENT QUESTIONARRIES

The SF-36 questionnaire used for Health-related Quality of life (HRQoL) assessment.

MEAN DATA OF SF36- PHYSICAL FUNCTIONING

Parameter	Variables
Baseline Assessment	30.67±7.04
Post cycle 1	94.00±4.71
Post cycle 2	94.33±4.95
Post cycle 3	95.00±5.00

MEAN DATA OF SF36- ROLE LIMITATIONS DUE TO PHYSICAL HEALTH

Parameter	Variables
Baseline Assessment	41.67±27.82
Post cycle 1	91.67±12.20
Post cycle 2	93.33±11.44
Post cycle 3	95.00±10.35

MEAN DATA OF SF36- ROLE LIMITATIONS DUE TO EMOTIONAL PROBLEMS

Parameter	Variables
Baseline Assessment	31.13±29.47
Post cycle 1	86.68±16.89
Post cycle 2	88.90±16.25
Post cycle 3	91.12±15.24

MEAN DATA OF ENERGY/FATIGUE

Parameter	Variables
Baseline Assessment	35.00±9.64
Post cycle 1	84.00±4.31
Post cycle 2	85.00±5.00
Post cycle 3	87.33±4.58

MEAN DATA OF EMOTIONAL WELL-BEING

Parameter	Variables
Baseline Assessment	34.40±6.90
Post cycle 1	88.53±5.83
Post cycle 2	90.40±5.62
Post cycle 3	91.73±3.53

MEAN DATA OF SF-36- SOCIAL FUNCTIONING

Parameter	Variables
Baseline Assessment	20.00±6.34

Post cycle 1	91.67±6.10
Post cycle 2	93.33±6.45
Post cycle 3	94.17±6.45
MEAN DATA OF SF 36- ON PAIN	
Parameter	Variables
Baseline Assessment	20.50±8.57
Post cycle 1	86.50±9.53
Post cycle 2	87.50±9.26
Post cycle 3	91.00±7.66
MEAN DATA OF SF36 ON GENERAL HEALTH	
Parameter	Variables
Baseline Assessment	21.00±4.31
Post cycle 1	86.50±9.53
Post cycle 2	89.17±7.42
Post cycle 3	94.00±7.25
MEAN DATA OF SF36- HEALTH CHANGE	
Parameter	Variables
Baseline Assessment	25.00±16.37
Post cycle 1	88.33±12.91
Post cycle 2	90.00±12.68
Post cycle 3	93.33±11.44

Table 2: EFFICACY ASSESSMENT ON HEALTH- RELATED QUALITY OF LIFE BY SF-36 PATIENT QUESTIONNAIRES

As shown in (table 2) In this study, interventions provided a significant improvement in Physical functioning, Social functioning, Energy/fatigue, regarding pain, regarding General Health, limitations due to physical health and limitations due to Emotional problems on health-related quality of life immediately after starting the treatment in subsequent three consecutive (post cycle 1, post cycle 2, post cycle 3) menstrual cycles

3.4.EFFICACY ASSESSMENT OF MENSTRUAL BLOOD LOSS BY PICTORIAL BLOOD LOSS ASSESSMENT SCORE

3.4a. PICTORIAL BLOOD LOSSASSESSMENT ON PADS

The mean score of Pictorial Blood Loss Assessment on Pads before the treatment of GRACE HING (Hing oil 15 mg) HPMC Capsules is 4.87±6.42.

The Average score of Pictorial Blood Loss Assessment on Pads after the treatment of GRACE HING (Hing oil 15 mg) HPMC Capsules in cycle 1 is 5.67 ± 6.11 , cycle 2 is 6.00 ± 6.21 and cycle 3 is 6.40 ± 7.28 .

In this study, interventions provides with increase in the amount of menstrual blood loss at each cycle after starting the treatment, however the amount of blood loss was within the normal limits and this effect was attributed to the emmenagogue property of the test product.

3.4b. PICTORIAL BLOOD LOSS ASSESSMENT ON TAMPOONS

The mean score of Pictorial Blood Loss Assessment on Tampons before the treatment of GRACE HING (Hing oil 15 mg) HPMC Capsules is 5.00 ± 6.11 .

The Average score of Pictorial Blood Loss Assessment on Tampons after the treatment of GRACE HING (Hing oil 15 mg) HPMC Capsules in cycle 1 is 5.87 ± 3.40 , cycle 2 is 5.93 ± 3.79 and cycle 3 is 6.20 ± 3.55 .

In this study, interventions provides with increase in the amount of menstrual blood loss at each cycle after starting the treatment, however the amount of blood loss was within the normal limits and this effect was attributed to the emmenagogue property of the test product.

3.4c. PICTORIAL BLOOD LOSS ASSESSMENT ON CLOTS

The mean score of Pictorial Blood Loss Assessment on Clots before the treatment of GRACE HING (Hing oil 15 mg) HPMC Capsules is 3.93 ± 1.83

The Average score of Pictorial Blood Loss Assessment on Clots after the treatment of GRACE HING (Hing oil 15 mg) HPMC Capsules in cycle 1 is 3.67 ± 1.95 , cycle 2 is 3.40 ± 2.03 and cycle 3 is 3.13 ± 2.07 .

3.4d. EFFICACY ASSESSMENT OF GRACE HING OIL BY ASSOCIATED SYSTEMIC SYMPTOMS

The study on Efficacy Assessment on Associated systemic symptom exhibited a decrease in the severity of systemic symptoms such as Fatigue, Nausea, Anorexia, Fever, Headache, Vertigo, Diarrhea, Vomiting, and Nervousness.

MEAN DATA OF ASSOCIATED SYSTEMIC SYMPTOMS

S.NO	Symptoms	Baseline assessment	Post cycle 1	Post cycle 2	Post cycle 3
1	Fatigue	2.20±0.68	0.73±0.70	0.60±0.63	0.53±0.64
2	Nausea	1.47±0.52	1.20±0.86	0.93±0.70	0.87±0.74
3	Anorexia	1.80±0.86	0.93±0.88	0.67±0.72	0.60±0.63
4	Fever	2.47±0.52	0.53±0.52	0.33±0.49	0.27±0.46
5	Headache	1.73±0.46	0.60±0.51	0.47±0.52	0.40±0.51
6	Vertigo	2.07±0.70	0.67±0.49	0.27±0.46	0.20±0.41
7	Diarrhoea	1.67±0.72	0.40±0.51	0.20±0.41	0.13±0.35
8	Vomiting	1.53±0.52	0.33±0.49	0.27±0.59	0.20±0.41
9	Nervousness	2.20±0.77	0.47±0.52	0.31±0.35	0.27±0.46

Table 3: MEAN DATA OF ASSOCIATED SYSTEMIC SYMPTOMS

As presented in table 3, the study on Efficacy Assessment on Associated systemic symptom exhibited a decrease in the severity of systemic symptoms such as Fatigue, Nausea, Anorexia, Fever, Headache, Vertigo, Diarrhoea, Vomiting, and Nervousness. The assessment on Analgesics usage have been reduced after starting the treatment in subsequent three consecutive (post cycle 1, post cycle 2, post cycle 3) menstrual cycles.

3.5. ANALGESIC USAGE:

The Average score of Analgesics usage in before the treatment of GRACE HING (Hing oil 15 mg) HPMC Capsules is 2.20±0.77.

The Average score of Analgesics usage in after the treatment of GRACE HING (Hing oil 15 mg) HPMC Capsules in cycle 1 is 0.73±0.59, cycle 2 is 0.47±0.52 and cycle 3 is 0.20±0.41.

The assessment on Analgesics usage have been reduced after starting the treatment in subsequent three consecutive (post cycle 1, post cycle 2, post cycle 3) menstrual cycles

4. DISCUSSION

Plants used for health care exhibit the largest biodiversity in terms of the basic needs of indigenous peoples.² It has been reported that about 64% of the total global population remains dependent on traditional medicine and medicinal plants for provision of their health-care needs⁶

In this study, we have covered one of the gynaecological diseases which women normally experience during their life time called primary dysmenhorrea.

Menstruation in women often causes unbearable pain. Though the Premenstrual syndrome takes the worst part, which is characterized by mild cramping and fatigue, but most of the time the

symptoms leave when your menstruation begins. However, much other serious menstrual adverse effect might be induced.⁷

Asafoetida usage is time immemorial in Indian medicine and culinary use as spice. It is also used in folk phytomedicine since ancient time in traditional medicine for the treatment of several neurological problems like hysterias epilepsy, paralysis, and depression, gastrointestinal problems, respiratory specially asthma and influenza, and reproductive disorders such as painful, difficult and excessive menstruation, premature labour, infertility and leucorrhoea ages ago, it relieve flatulence, relieve spasm of involuntary muscle, digestive, increase menstrual flow, sedative, aphrodisiac properties. These days hypotensive, antinociceptive, free radical scavenging, antispasmodic, neuroprotective, stimulate sexual desire, antiviral, reduce anxiety, antidiabetic, gastric anti-ulcer, antiseptic, nephroprotective, and anticarcinogenic properties are proven the beneficial effect of the drug and alleviation and both in animal and humans.⁹

This study suggests that GRACE HING (Hing oil 15 mg) HPMC Capsules represents a safe, effective treatment for menstrual pain, its associated systemic symptoms and to improve health-related quality of life and without significant side effect.

5. CONCLUSION

The use of GRACE HING (Hing oil 15 mg) HPMC Capsules for dysmenorrheic women was shown to be effective in regard to a reduction in the common symptoms associated with dysmenorrhea, furthermore without any significant side effects in the therapeutic doses used in this study.

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